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Exploring the Role of Isoproterenol in Atrioventricular Blocks Management: A Literature Review

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Abstract:

Atrioventricular (AV) block is a condition characterised by impaired conduction of impulses between atria and ventricles with varying degrees of severity. Isoproterenol, a non-selective beta-adrenergic agonist, is used in the treatment of AV blocks, especially in cases of Mobitz type 2 and complete heart blocks. Its mechanism in patients with AV blocks is increasing A-V nodal conduction. Isoproterenol has shown efficacy in the management of hemodynamically unstable patients with Mobitz type 2 and third-degree AV block while waiting for permanent pacemaker placement. It has been approved for heart blocks where a pacemaker is not needed and for cardiac arrest caused by heart block where pacemaker treatment is not an option. It has many potential side effects such as increased heart rate, hypotension, and myocardial ischemia, therefore, careful monitoring is necessary. Summarizing it, isoproterenol has a vital role in treating AV blocks and offers an alternative drug in both acute management and long-term treatment options.

However, future research is needed to compare the safety and efficacy of isoproterenol which could help make the best treatment strategies in patients with AV blocks.

keywords: isoproterenol, isoprenaline, atrioventricular block, atrioventricular blocks, AV blocks

Background:

Atrioventricular (AV) block is a condition characterized by impaired conduction impulses between atria and ventricles. It can be partial or complete and has been divided into three types; first-degree, second-degree, and third-degree AV blocks. First-degree AV block involves prolongation of PR interval with no beat drop on the ECG surface and requires no specific treatment. (1) Second-degree AV block is divided into two types, Mobitz type-1, also known as Wenckebach and Mobitz type-2. The existing knowledge has defined second-degree AV block in different ways, especially Wenckebach.(2) Mobitz type-1 involves a progressive increase in the PR interval until a drop beat and requires no specific treatment.(1) Mobitz type 2 involves blockage of conduction of one or more P waves with no change in the PR interval before and after the nonconducted P waves.(2) Third-degree AV block involves complete blockage of atrial electrical impulses reaching the ventricular conduction system. However, the P-P and R-R intervals will remain the same. Mobitz type 2 and third-degree AV blocks can be managed therapeutically by isoproterenol, atropine, dopamine, and epinephrine, however, if the AV block is high grade then it requires permanent pacemaker placement.(3)

Isoproterenol is a non-selective beta-receptor agonist, hence, has sympathomimetic properties. It can cause bronchodilation and vasodilation, thus used as a treatment option in the management of asthma and hypertension respectively.(4),(5),(6),(7) It also decreases vagal tone at the AV node, therefore, it is used in the acute management of Mobitz type 2 and complete heart blocks.(2),(5) A recent study on the effects of isoproterenol has proved the effects of isoproterenol on increasing atrioventricular conduction. (8)

The main aim of this review is to explore the use as well as efficacy and safety of isoproterenol in the management of AV blocks so that a better understanding of existing literature is provided. This study can be useful for teachers, students, and researchers because it would help them understand how isoproterenol is used to treat nodal blocks, and thus would be helpful in the advancement of cardiovascular medicine and patient care. It also provides understanding to fill the knowledge gaps in already known literature. However, further research and clinical studies are needed for its widespread use.

Isoproterenol and AV blocks:

Isoproterenol is a sympathomimetic drug and acts as a synthetic nonselective beta-adrenergic agonist. It has a positive chronotropic effect on the heart due to its beta-1 agonist properties thus increasing the sinus rate and enhancing A-V nodal conduction, hence, it can be used in the management of AV blocks. (9) It has bronchodilatory and vasodilatory effects due to its beta-2 receptor agonism properties and thus can be used to manage other disorders like asthma and hypertension in patients experiencing AV blocks. (4),(5),(10)

Isoproterenol infusion is the best option for acute management of hemodynamically unstable Mobitz type 2 and third-degree atrioventricular (AV) block while waiting for permanent pacemaker placement. It is widely used along with dopamine as a combination therapy for the management of AV block. (11) Recent studies show the efficacy of isoproterenol in the improvement of AV blocks. (12) Thus, it has been reported to be more effective than dopamine in achieving a positive clinical response and reduces the need for temporary artificial pacing in patients experiencing AV blocks. (13) It has been demonstrated that isoproterenol use is safe and well-tolerated because no induction of arrhythmia or any hypotensive issues have been reported. Moreover, it increases the heart rate of pacemaker-dependent patients who are undergoing pacemaker replacement by reducing the need for temporary transvenous pacemaker positioning. (14) As clinical data suggests, isoproterenol infusion is a more effective, safer, and better-tolerated treatment option for managing unstable Mobitz type 2 and third-degree AV block in emergencies until a permanent pacemaker can be implanted.(3)

While using isoproterenol in the management of certain types of atrioventricular (AV) block, it can cause potential adverse effects if not monitored carefully. Due to its beta-1 adrenergic receptor agonist property, it can increase the heart rate, which is beneficial for bradycardic AV block but may cause hemodynamic instability, palpitations, and predispose patients to various cardiac arrhythmias including ventricular and supraventricular tachycardia. (15) It can cause peripheral vasodilation by stimulating beta-2 adrenergic receptors in vascular smooth muscle. This vasodilation results in decreased systemic vascular resistance, which can cause hypotension, especially in patients with decreased vascular tone or pre-existing hypotension. (16),(17) It also causes an increase in heart rate and myocardial oxygen demand, therefore, it may worsen myocardial ischemia, especially in patients with underlying coronary artery disease. (18) Long-term use of the drug can lead to cardiac remodeling which is characterized by myocardial hypertrophy, interstitial fibrosis, and dilation of cardiac chambers, thus can lead to heart failure. It is mainly used in combination with dopamine and, thus, can cause adverse effects such as nausea and vomiting, hence, can complicate invasive procedures, such as the implantation of a pacemaker. (11)

Isoproterenol has beneficial effects in managing atrioventricular blocks due to its effectiveness in restoring normal heart rhythms, stabilizing cardiac function, and addressing specific arrhythmias associated with AV blocks. Due to beta-1 agonism property, it has been used for bradyarrhythmias and heart blocks for many years. (2),(19),(20) Heart blocks like Mobitz type 2 and complete heart blocks are managed acutely with isoproterenol.(5) Many patients with atrioventricular block do not require rapid stabilization, however, isoproterenol can be considered as a treatment option if the patient is symptomatic with a depressed ventricular rate. (3) It has been proven that isoproterenol has a more satisfactory effect in achieving a clinical response thus, reducing the need for temporary artificial pacemaker placement. (13) Therefore, it can be an alternative drug in both acute management and long-term treatment options in patients with AV blocks. However, future research is needed to compare the safety and efficacy of isoproterenol which could help make the best treatment strategies in patients with AV blocks.

The use of isoproterenol in treating atrioventricular block is based on recent research findings and is effective in treating symptomatic bradycardia, such as complete atrioventricular block. Although it is not currently included in treatment guidelines, it is still a valid option. Studies have demonstrated that isoproterenol infusions have a lower incidence of side effects compared to other medications like dopamine, which reduces the need for temporary delay while waiting for definitive pacemaker implantation. (13),(21) While the current guidelines recommend atropine, and dopamine/epinephrine as first-line treatments for AV blockade, beta-adrenergic agonists like isoproterenol provide better benefits than other pharmacological drugs. Conducting studies that evaluate the effects of long-term beta-adrenergic stimulation on cardiac function, remodeling, and clinical outcomes could be the best option for the timing and duration of treatment. Further studies comparing the safety and efficacy of isoproterenol in AV block patients may help establish the best treatment strategies and could lead to the widespread use of isoproterenol in AV block treatment procedures in the future. (22) However, further research and clinical trials are required to be performed for its prophylactic use.

Conclusion:

In conclusion, isoproterenol has an important role in the treatment of AV block, especially in Mobitz type 2 and complete heart block. Its mechanism in managing AV blocks is to improve A-V nodal conduction. Therefore, it has been useful for short-term treatment while waiting for permanent pacemaker implantation. Despite potential side effects, isoproterenol can be the best treatment option and indicates the potential as a long-term treatment option for AV block. However, further research and clinical studies are needed for its widespread use.

List of Abbreviations:

AV (Atrioventricular)

PR (Interval between P and R wave)

PP (Interval between two P waves)

RR (Interval between two R waves)

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References:

1. Gomes JAC, El-Sherif N. Atrioventricular block. Mechanism, clinical presentation, and therapy. Med Clin North Am [Internet]. 1984;68(4):955–67. Available from: http://dx.doi.org/10. HYPERLINK "http://dx.doi.org/10.1016/S0025-7125(16)31108-7" HYPERLINK "http://dx.doi.org/10.1016/S0025-7125(16)31108-7" HYPERLINK "http://dx.doi.org/10.1016/S0025-7125(16)31108-7"1016/S0025-7125(16)31108-7
2. Serge Barold S, Hayes DL. Second-degree atrioventricular block: A reappraisal. Mayo Clin Proc. 2001;76(1):44–57.
3. Saleh F, Greene EA, Mathison D. Evaluation and management of atrioventricular block in children. Curr Opin Pediatr. 2014;26(3):279–85.
4. Vargas G, Akhtar M, Damato AN. Electrophysiologic effects of isoproterenol on cardiac conduction system in man. Am Heart J. 1975;90(1):25–34.
5. Gump A, Haughney L, Fredberg J. Relaxation of activated airway smooth muscle: Relative potency of isoproterenol vs. tidal stretch. J Appl Physiol. 2001;90(6):2306–10.
6. YEAGER H, WEINBERG RM, KAUFMAN L V., KATZ S. Asthma: Comparative Bronchodilator Effects of Ipratropium Bromide and Isoproterenol. J Clin Pharmacol. 1976;16(4):198–204.
7. Valentine. Asthmatic Patients. Anesthesiology. 1971;34(5):420–420.
8. Ota M. NII-Electronic Library Service. Chem Pharm Bull [Internet]. 1970;(43):2091. Available from: http://www.mendeley.com/research/geology-

volcanic-history-eruptive-style-yakedake-volcano-group- HYPERLINK "http://www.mendeley.com/research/geology-volcanic-history-eruptive-style-yakedake-volcano-group-central-japan/" HYPERLINK "http://www.mendeley.com/research/geology-volcanic-history-eruptive-style-yakedake-volcano-group-central-japan/" HYPERLINK "http://www.mendeley.com/research/geology-volcanic-history-eruptive-style-yakedake-volcano-group-central-japan/"central-japan/

9. Tantaka H, Clark RB, Giles WR. Positive chronotropic responses of rabbit sino-atrial node cells to flash photolysis of caged isoproterenol and cyclic AMP. Proc R Soc B Biol Sci. 1996;263(1368):241–8.

10. Bull M, Shelke, A. R. , Roscoe, J. A. , Morrow, G. R. , Colman, L. K. , Banerjee, T. K. , & Kirshner JJ. 基因的改变 NIH Public Access. Bone [Internet]. 2008;23(1):1–7. Available from: https://www.ncbi.n HYPERLINK "https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2688697/pdf/nihms-110443.pdf" HYPERLINK "https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2688697/pdf/nihms-110443.pdf" HYPERLINK "https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2688697/pdf/nihms-110443.pdf"lm.nih.gov/pmc/articles/PMC2688697/pdf/nihms-110443.pdf

11. 二十七、Rooks, M.G and Garrett, W.S 2016. 乳鼠心肌提取 HHS Public Access. Physiol Behav. 2017;176(3):139–48.

12. Dhingra RC, Winslow E, Pouget JM, Rahimtoola SH, Rosen KM. The effect of isoproterenol on atrioventricular and intraventricular conduction. Am J Cardiol. 1973;32(5):629–36.

13. De Lazzari M, Martini N, Migliore F, Donato F, Babuin L, Tarantini G, et al. Efficacy and Safety of Isoprenaline during Unstable Third-Degree Atrioventricular Block. J Cardiovasc Dev Dis. 2023;10(12):1–10.

14. Chihrin SM, Mohamed U, Yee R, Gula LJ, Klein GJ, Skanes AC, et al. Utility of Isoproterenol in Unmasking Latent Escape Rhythm in Pacemaker Dependent Patients Undergoing Pacemaker Replacement. Am J Cardiol. 2008;101(5):631–3.

15. Patel PJ, Segar R, Patel JK, Padanilam BJ, Prystowsky EN. Arrhythmia induction using isoproterenol or epinephrine during electrophysiology study for supraventricular tachycardia. J Cardiovasc Electrophysiol. 2018;29(12):1635–40.

16. Ehlers TS, van der Horst J, Møller S, Piil PK, Gliemann L, Aalkjær C, et al. Colchicine enhances β adrenoceptor-mediated vasodilation in men with essential hypertension. Br J Clin Pharmacol. 2023;89(7):2179–89.

17. Oberoi GS, Saini SS. Induced hypotension in a smoker. P N G Med J. 1994;37(4):224–5.

18. Hatle L, Rokseth R. Conservative treatment of AV block in acute myocardial infarction. Results in 105 consecutive patients. Br Heart J. 1971;33(4):595–600.

19. Zappa D, Herman LL. ORAL bo ds ORAL bo ds. 2022;1–29.

20. Headrick JP, Gauthier NS, Morrison RR, Matherne GP. Chronotropic and vasodilatory responses to adenosine and isoproterenol in mouse heart: Effects of adenosine A1 receptor overexpression. Clin Exp Pharmacol Physiol. 2000;27(3):185–90.

21. Su LN, Wu MY, Cui YX, Lee CY, Song JX, Chen H. Unusual course of congenital complete heart block in an adult: A case report. World J Clin Cases. 2022;10(19):6602–8.

22. Kusumoto FM, Schoenfeld MH, Barrett C, Edgerton JR, Ellenbogen KA, Gold MR, et al. 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Vol. 140, Circulation. 2019. 382–482 p.