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EFFICACY OF B-BLOCKERS IN CONGESTIVE HEART FAILURE

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ABSTRACT

Background & Purpose: Beta blocking drugs have been proven to lessen the danger of hospitalization and demise in patients with slight-to-moderate congestive heart failure, but little is understood about the efficacy or protection of these drugs in excessive heart failure. The Aim of this work is to provide cumulative data about the effect of β-Blockers on morbidity and mortality outcomes in Congestive Heart Failure (CHF) patients. **Methods:** A systematic search was performed of PubMed, Cochrane library Ovid, Scopus & Google scholar to identify family medicine RCTs, clinical trials, and comparative studies, which studied the outcome of B-blocker group versus Placebo group of CHF patients. A meta-analysis was done using fixed and random-effect methods. The primary outcome was mortality rate (of any cause). Secondary outcome was hospital admission due to CHF. **Results:** A total of 5 studies were identified involving 12785 patients, 6402 patients in B-blocker group, and 6343 patients in Placebo group. Regarding outcome measured, meta-

analysis study showed that, highly significant increase in mortality and hospitalization for CHF in placebo group as compared to B blocker group, with a combined risk ratio (RR) of 1.4 and 1.35 respectively ($P < 0.01$). **Conclusion:** To conclude, the beta blockers proved to be very effective in lowering mortality and the need for hospital admission due to HF patients.

KEYWORDS: B Blockers, CHF.

INTRODUCTION

The Congestive heart failure (CHF) is a critical clinical situation where the heart can't pump the blood needed for the whole body. CHF is regularly caused by hypertension, diabetes, or coronary heart disease.[1]

Congestive heart failure (CHF) remains to be one of the major cardiovascular disorders. Regardless its excessive expenditure in healthcare budgets, the mortality fee of CHF patients may be up to 8 times higher than the age matched manage populace.[2] Congestive Heart failure sufferers revel in signs and symptoms of fatigue and absence of energy, dyspnea, depression, pain, and cognitive impairment, amongst different troubles. despite the fact that maximum patients have worsened dyspnea with episodes of volume overload, HF associated dyspnea and exertional fatigue are not immediately associated with pulmonary capillary wedge pressure or cardiac output, rather to broader, systemic effects of HF, inclusive of generalized myopathy.[3]

The existing treatment protocols of CHF sufferers, including administrating angiotensin converting enzyme inhibitors (ACE-I) and β blockers, were tested to lower the mortality and hospital admission cost. Though, the residual danger for mortality and morbidity of CHF stays high even underneath such remedy protocols.[2]

Beta-blockers are the main treatment in heart failure. In CHF, sympathetic hyperactivation may cause shortening of left ventricular diastolic filling, accelerated tachy-arrhythmias and hypertension. To this effect, beta-blockers can reverse the neurohormonal consequences of sympathetic nervous system and might offer advantage in patients with CHF.[4]

Especially, β adrenergic blockers have been shown in clinical trials to improve survival, decrease arrhythmia, improve signs of heart failure and left ventricular ejection fraction, and manipulate ventricular price, especially in sufferers with persistent congestive heart failure.[5]

Many HF patients and reduced ejection fraction die.[6] Beta blocking drugs have been proven to lessen the danger of hospitalization and demise in patients with slight-to-moderate congestive heart failure, but little is understood about the efficacy or protection of these drugs in excessive heart failure.[7]

In sufferers with systolic heart failure and in sinus rhythm included within the SHIFT (Systolic Heart failure treatment with the inhibitor ivabradine Trial) study, congestive heart rate has been diagnosed as a modifiable hazard element. Heart rate 70 beats/min in sufferers treated with a beta-blocker, as well as in those without a beta-blocker due to loss of tolerability of the drug, turned into determined to be strongly associated with the hazard of worsening of heart failure or demise because of heart failure.[8]

Aim of the study

The Aim of this work is to provide cumulative data about the effect of β-Blockers on morbidity and mortality outcomes in Congestive Heart Failure (CHF) patients.

METHODS

This review was carried out using the standard methods mentioned within the Cochrane handbook and in accordance with the (PRISMA) statement guidelines.[9]

Identification of studies

- An initial search carried out throughout the PubMed, Cochrane library Ovid, Scopus & Google scholar using the following keywords: β-Blockers and Congestive Heart Failure.
- We will consider published, full text studies in English only. Moreover, no attempts were made to locate any unpublished studies nor non-English studies.

Criteria of accepted studies

- **Types of studies**

The review will be restricted to RCTs, clinical trials, and comparative studies, either prospective or retrospective, which studied the outcome of B-blocker group versus Placebo group of CHF patients.

- **Types of participants:** CHF patients.
- **Types of outcome measures**

1. Primary outcome is to measure the rate of hospital admission for CHF.
2. Secondary outcome is to measure the rate of mortality.

Inclusion criteria

- ✓ English literature.
- ✓ Journal articles.
- ✓ Between 2000 until 2012.
- ✓ Describing RCTs or clinical trials with either B-blocker group or Placebo group.
- ✓ Human studies.

Exclusion criteria

- ✓ Articles describing other drugs for treatment of heart failure.
- ✓ Irrelevance to our study

Methods of the review

■ **Locating studies**

Abstracts of articles identified using the above search strategy will be viewed, and articles that appear of fulfill our inclusion criteria will be retrieved in full, when there is a doubt, a second reviewer will assess the article and consensus will be reached.

■ **Data extraction**

Using the following keywords: β-Blockers and Congestive Heart Failure, data will be independently extracted by two reviewers and cross-checked.

Statistical analysis

Statistical analysis done using MedCalc ver. 18.11.3 (MedCalc, Ostend, Belgium). Data were pooled and risk ratios (RRs) as well as standard mean differences (SMD), were calculated with their 95 per cent confidence intervals (CI). A meta-analysis was performed to calculate direct estimates of each treatment, technique or outcome. According to heterogeneity across trials using the I^2-statistics; a fixed-effect model ($P \geq 0.1$) or random-effects model ($P < 0.1$) was used.

Study selection

We found 138 record; 84 were excluded based on title and abstract review; 54 articles are searched for eligibility by full text review; 28 articles cannot be accessed or obtain full text; 10 studies were reviews and case reports; 11 were not describing functional outcome; leaving 5 studies that met all inclusion criteria (Fig. 1).

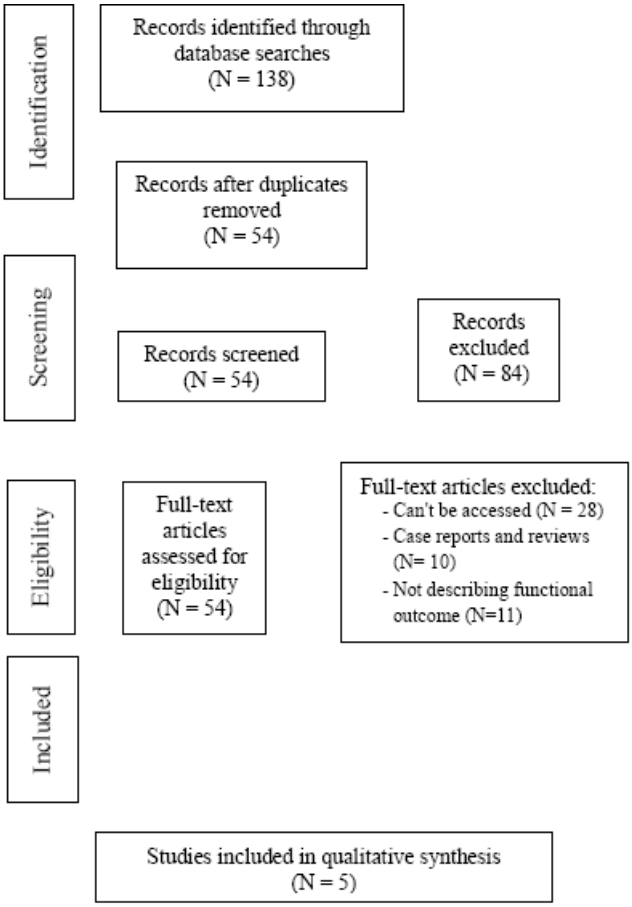

Figure 1: Flow chart for study selection.

RESULTS

Descriptive analysis of all studies included (Table 1, 2)

Table 1: Patients and study characteristics.

N	Author	Type of study	Total	Number of patients B-blocker group	Placebo group	Age (average years)	HTN	DM	IHD	Stroke
1	***Hjalmarson et al., 2000***	Retrospective	3991	1990	2001	63.8	1756	977	2614	---
2	***Joglar et al., 2001***	Retrospective	136	84	52	64.5	---	---	69	---
3	***Lechat at al., 2001***	Retrospective	2539	1271	1268	62	403	330	1264	304
4	***van Veldhuisen et al., 2006***	Retrospective	3991	1990	2001	65	1827	985	2607	314
5	***Mulder et al., 2012***	Retrospective	2128	1067	1021	77	1312	555	1452	---

#Studies were arranged according to publication year.

Table 2: Summary of outcome measures in all studies.

N	Author	Outcomes			
		Rate of mortality		Rate of hospital admission for CHF	
		B-blocker group	Placebo group	B-blocker group	Placebo group
1	***Hjalmarson et al., 2000***	145	217	200	145
2	***Joglar et al., 2001***	4	6	6	4
3	***Lechat at al., 2001***	102	146	110	102
4	***van Veldhuisen et al., 2006***	30	58	581	30
5	***Mulder et al., 2012***	169	192	143	169

All studies that has been included in this metanalysis between 2000 and 2012 were retrospective. The total number of patients in all the included studies was 12785 patients, with 6402 patients in B-blocker group, and 6343 patients in Placebo group.

The average age of all patients was (66.4 years); with youngest mean age of 62 years in Lechat at al., 2001 study; and oldest mean age of 77 years in Mulder et al., 2012 study.

Regarding other patients' characteristics, 3986 (31.1%) patients had HTN, 2292 (17.9%) patients had DM, 6554 (51.2%) patients had IHD, and 618 (4.8%) patients had strokes.

Outcome measures

Regarding outcome measures, all 5 studies reported mortality and hospitalization rates.

Meta-analysis of outcome measures

Data were divided into two groups:

1) B-blocker group
2) Placebo group

Meta-analysis study was done on 5 studies which described and compared the 2 different groups of patients; with overall number of patients (N=12785).

Patients who reached adverse outcomes were pooled:

Each outcome was measured by

✓ **Relative Risk or Risk Ratio (RR)**

- For mortality rate.
- For hospitalization rate.

Regarding mortality outcome measure (Fig. 2);

I2 (inconsistency) was 35% with non-significant Q test for heterogeneity ($p > 0.05$), so fixed-effects model was done; with overall RR= 1.4.

The fixed-effects model of the meta-analysis study showed highly significant increase in mortality rate, in placebo group compared to B-blocker group ($p < 0.01$).

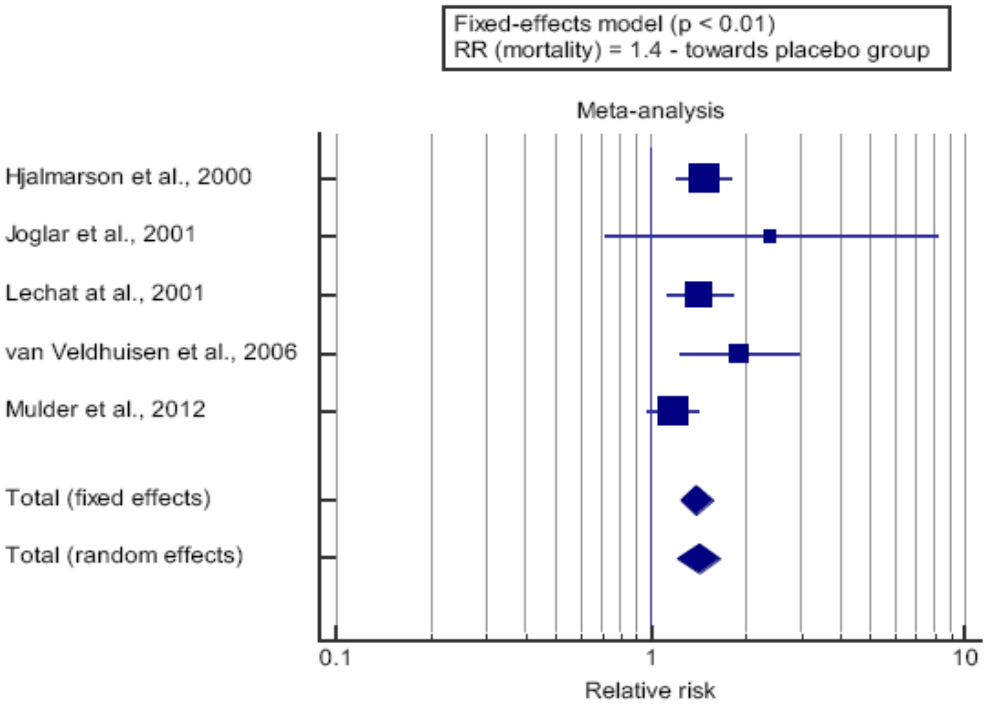

Figure 2: Forest plot of (mortality rate) on B-blocker group vs Placebo group – Risk Ratio.

Regarding hospitalization for CHF outcome (Fig. 3);

I2 (inconsistency) was 81% with highly significant Q test for heterogeneity ($p = 0.0002$), so random- effects model was carried out; with overall RR= 1.35.

Meta-analysis study showed that; random-effects model showed highly significant increase in hospitalization rate for CHF, in placebo group compared to B-blocker group ($p = 0.005$).

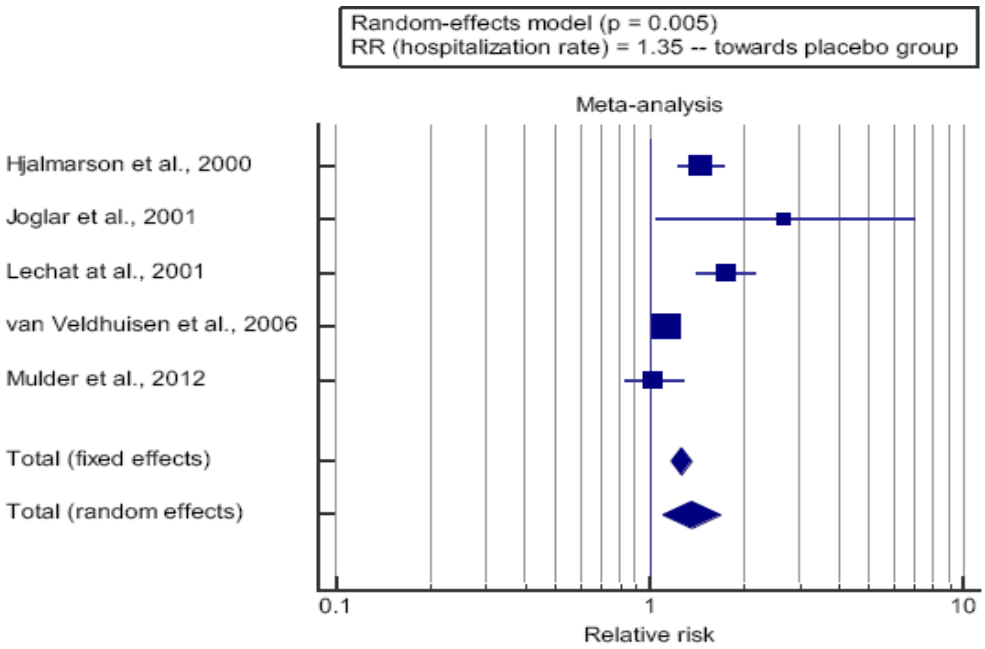

Figure 3: Forest plot of (hospitalization rate) on B-blocker group vs Placebo group – Risk Ratio.

DISCUSSION

The Aim of this work is to provide cumulative data the effect of β-Blockers on different outcomes in Congestive Heart Failure (CHF) patients.

The average age of all patients was (66.4 years); which came in agreement with ***Grayburn et al. 2005***[10] and ***Cadrin-Tourigny et al. 2017.***[11]

Grayburn et al. 2005 reported that the range of age for all patients was 60 ± 13 years.

Regarding other patients' characteristics, 314 patients had HTN, 177 patients had DM, 487 patients had IHD, and 44 patients had strokes, which came in agreement with ***Rienstra et al., 2013,*** who reported in his meta-analysis that, IHD was the most common etiologic factor in CHF patients.[16]

Regarding outcome measures, all 5 studies reported mortality and hospitalization rates.

Regarding mortality outcome measure; fixed-effects model of the meta-analysis study showed highly significant increase in mortality rate, in placebo group compared to B-blocker group ($p < 0.01$), which came in agreement with ***Hjalmarson et al. 2000***[12] and in disagreement with the ***(Trial of the Beta-Blocker Bucindolol in Patients with Advanced***

Chronic Heart Failure" 2001).[13]

Hjalmarson et al. 2000 reported that the incidence of mortality was lower in metoprolol group (641) than in placebo group (767) with risk reduction 19%, with $p < 0.001$.

"A Trial of the Beta-Blocker Bucindolol in Patients with Advanced Chronic Heart Failure" 2001[13] reported that there was non-significant difference in mortality rate between the two study groups ($p > 0.05$).

Regarding hospitalization for CHF outcome, meta-analysis study showed that; random-effects model showed highly significant increase in hospitalization rate for CHF, in placebo group compared to B-blocker group ($p < 0.05$) which came in agreement with ***Shibata, Flather, and Wang 2001***[14] and in disagreement with ***Flather et al. 2005.***[15]

Shibata, Flather, and Wang 2001 reported that Hospitalizations occurred in 613/5301 (11.5%) and 833/4827 (17.2%) in active and placebo groups, respectively, OR 0.63, $P < 0.001$.

Flather et al. 2005 reported that There was no difference between the groups for hospitalization for heart failure [placebo 144 (13.7%), nebivolol 145 (13.9%); $P < 0.05$].

In another big meta-analysis conducted with the aid of ***Rienstra et al., 2013***, which covered 8680 cases with HF, there had been 842 cases administered with beta-blocker, and 835 with placebo. In AF cases, betablockade did now not lessen mortality (OR: 0.86; $p > 0.05$), whilst in sinus rhythm cases, there has been a giant reduction (OR: 0.63; $p < 0.01$). interaction analysis confirmed substantial interaction of the effects of beta-blocker treatment in AF as opposed to that during sinus rhythm ($p < 0.05$). by using meta-regression evaluation, they did not discover confounding by all relevant covariates. Betablocker therapy was not related to a reduction in HF hospitalizations in AF (OR: 1.11; $p > 0.05$), in comparison to sinus rhythm (OR: 0.58; $p < 0.01$). there has been a substantial interaction of the effects of beta-blocker therapy in AF versus that in sinus rhythm ($p < 0.01$).[16]

CONCLUSION

To conclude, the beta blockers proved to be very effective in lowering mortality and the need for hospital admission due to HF patients.

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Conflict of interest

None.

Authorship

All the listed authors contributed significantly to conception and design of study, acquisition, analysis and interpretation of data and drafting of manuscript, to justify authorship.

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