Prescription pattern and rationality of antihypertensive drugs in patients of type 2 diabetes with hypertension: a pilot study

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ABSTRACT

Background: As presence of hypertension (HTN) in type 2 diabetes significantly increases risk of morbidity and mortality, its control with rational use of antihypertensives is essential. Authors performed this study to understand the current prescribing pattern of antihypertensives in patients of type 2 diabetes and their assess the rationality to recommendations of JNC-8 guidelines.

Methods: Authors performed a cross sectional survey of prescription of diagnosed patients of diabetes with HTN at a tertiary care hospital. Prescription of patients attending medicine OPD were scanned. Data was collected over 2 month and analyzed with descriptive statistics.

Results: In 76 patients analysed, mean age was 54.9±9.3 years and 51.3% were females. Insulin and oral antidiabetic agents were prescribed in 16 (21.1%) and 73 (96.1%) patients respectively. One, two, three and four antihypertensive drugs were prescribed in 44 (57.9%), 28 (36.8%), 3 (3.9%) and 1 (1.3%) patients respectively and 24 (31.6%) of them were fixed dose combinations. Among antihypertensives, angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), thiazide diuretics, beta blockers (BBs) and calcium channel blockers (CCBs) were present in 29 (38.2%), 26 (34.2%), 22 (28.9%), 21 (27.6%) and 14 (18.4%) respectively. In individual drugs, ramipril (28.9%) was most common followed by telmisartan (26.3%), hydrochlorothiazide (26.3%), atenolol (16, 21.1%) and amlodipine (17.1%) were frequently prescribed. In adjuvant drugs, antiplatelet (52.6%) and statins (56.6%) were common. This pattern of prescription was as per the recommendations of recent JNC-8 guidelines for treatment of hypertension.

Conclusions: ACEIs/ARB are the most preferred for HTN treatment in type 2 diabetes mellitus. Prescription of antihypertensives in our set up was rational as per JNC-8 recommendations.

Keywords: Guidelines, Hypertension, Prescription, Type 2 diabetes
<140/90 is advised by the most guidelines in patients T2DM.\(^6\)

Achievement of better control of HTN in patients with T2DM is possible with use of multiple anti-hypertensive medications. Among these, ACEIs/ARBs, CCBs and thiazide diuretics are recommended as first line agents in T2DM.\(^5\)

Despite availability of multiple effective antihypertensive drugs, control of HTN remains poor.\(^7\) Therefore, assessment of drug prescribing pattern is necessary to ascertain that the current trends are according to guideline recommendations. This can identify any deviations from recommended therapy and help to take corrective measures.

Different studies have demonstrated that prescribing patterns of antihypertensive in T2DM are as per the international recommendations.\(^8,9\) Understanding the prescribing practices help identify gaps in adequate therapy for control of HTN which is important especially in patients with T2DM. However, there have been no studies conducted at our institute to understand the prescribing pattern of antihypertensives in T2DM patients. Hence, authors planned this cross-sectional study.

**METHODS**

The study was conducted in patients of T2DM with HTN attending the medicine outpatient department (OPD) of a tertiary care hospital.

Ethical approval was taken from institutional ethics committee approved the protocol for the study. A cross-sectional, single centre, observational study at the medicine outpatient setting.

**Inclusion criteria**

- Patients of age ≥18 years,
- Both genders,
- Diagnosed as type 2 diabetes mellitus with hypertension by the physician,
- Has been prescribed treatment for HTN.

**Exclusion criteria**

- Patients requiring admission to the hospital,
- Pregnant and lactating women,
- Patient not willing to reveal their prescription data.

After taking the informed consent from the patients, the data from their prescription was recorded in case record form (CRF). The data collected includes demographic data like age, gender, and details of the drugs prescribed. Prescription of patients with T2DM and HTN in one-month duration were captured.

**Parameters assessed**

Total number of drugs per prescription was calculated. Among medications for T2DM and HTN, total number, drug class, individual drugs, dose and frequency of administration were recorded. Also, total number of drugs per prescription was calculated by counting all the drugs in prescription.

**Assessment of rationality to guidelines**

The prescribed treatment for HTN was then compared with recommendations of JNC-8 guidelines\(^5\) to ascertain whether treatment was as per the recommendations or not.

**Statistical analysis**

The captured data was entered into Microsoft excel sheet version 2010. Data was analyzed with descriptive statistics in excel sheet only. Categorical variables were presented as frequency and percentages. Continuous variables were presented as mean and standard deviation.

**RESULTS**

**Baseline characteristics**

In one-month prescription data captured in CRF, total 76 patients were included. Mean age of the patients was 54.9±9.3 years and most of them were in age group of 51-60 years. Proportion of females was 51.3% (Table 1). Provides demographic characteristics of the patients.

| Parameter          | Observation (%) |
|--------------------|-----------------|
| Age (years)        |                 |
| Mean±SD            | 54.9±9.3        |
| Age groups         |                 |
| <40                | 6 (7.9)         |
| 41-50              | 20 (26.3)       |
| 51-60              | 27 (35.5)       |
| >60                | 23 (30.3)       |
| Sex                |                 |
| Male               | 37 (48.7)       |
| Female             | 39 (51.3)       |

**Total number of drugs per prescription**

Figure 1 shows that most prescriptions contained 5 to 7 drugs (51.3%) in total followed by ≤5 drugs (23.7%) and 8 to 10 drugs (19.7%).

**Oral antidiabetic agents prescribing pattern**

Metformin (80.3%), sulfonylureas (68.4%) and alpha glucosidase inhibitors (26.3%) were common antidiabetic drugs prescribed in study patients (Table 2).
As outlined in Table 4, ramipril (28.9%), telmisartan (17.1%), hydrochlorothiazide (26.3%), atenolol (21.1%) and amlodipine (17.1%) were the common drugs prescribed form their antihypertensive class.

**Table 4: Prescribing frequency of individual antihypertensive drugs.**

| Antihypertensive drugs | Observation (%) |
|------------------------|-----------------|
| ACEIs                  |                 |
| Ramipril               | 22 (28.9)       |
| Enalapril              | 5 (6.6)         |
| Lisinopril             | 2 (2.6)         |
| ARBs                   |                 |
| Telmisartan            | 13 (17.1)       |
| Losartan               | 12 (15.8)       |
| Olmesartan             | 1 (1.3)         |
| Thiazide diuretics     |                 |
| Hydrochlorothiazide    | 20 (26.3)       |
| Chlorthalidone         | 2 (2.6)         |
| Beta-blockers          |                 |
| Atenolol               | 16 (21.1)       |
| Metoprolol             | 4 (5.3)         |
| Carvedilol             | 1 (1.3)         |
| CCB                    |                 |
| Amlodipine             | 13 (17.1)       |
| Nifedipine             | 1 (1.3)         |

**Concomitant drugs**

Among concomitant medications, antiplatelet and hypolipidemic drugs were prescribed in 52.6% and 56.6% patient respectively. Aspirin was prescribed in all cases either as single drug (39.5%) or in combination with clopidogrel (13.2%). Rosuvastatin and atorvastatin were prescribed with near equal frequency as shown in (Table 5).

**Table 5: Details of other drugs prescribed.**

| Drugs                | Observation (%) |
|----------------------|-----------------|
| Antiplatelets        | 40 (52.6)       |
| Aspirin              | 30 (39.5)       |
| Aspirin + Clopidogrel| 10 (13.2)       |
| Hypolipidemic        | 43 (56.6)       |
| Rosuvastatin         | 22 (28.9)       |
| Atorvastatin         | 21 (27.6)       |

**Rationality of antihypertensive drugs**

As per JNC-8 guidelines5, ACEIs/ARBs, Thiazide diuretics or CCBs are among the preferred choices for management of HTN in patients with T2DM. Authors observed similar pattern with most common use of ACEIs/ARBs, thiazide diuretics and CCBs in total covering treatment of over 80% patient of T2DM with HTN.
DISCUSSION

In this study, mean age of the patients was 54.9±9.3 years suggesting patients who are above 50 years of age have higher propensity of development of cardiometabolic disorders like HTN and T2DM. Most patients received metformin, sulfonylureas and insulin which are cornerstone of T2DM treatment since past many decades. In India, these are most frequently prescribed anti-diabetic agents. A study from Indore city in India identified similar pattern of antidiabetic drug prescription where metformin and glimepiride were the most frequently prescribed drugs. Another study from Navi Mumbai also reported that metformin dominated the antidiabetic therapy. This is according to the American diabetes association (ADA) guidelines recommendations where metformin is advised as a first choice of drug for treatment of T2DM. In present study, prescription of single or two antihypertensive agents was more common. A study from Shekar AM form India reported that prescription of antihypertensive monotherapy was more common than polytherapy (60.14% vs 39.86% respectively) in patients with diabetes. Study from Ethiopia by Abegaz et al, reported monotherapy in 50% of the patients. Dhanraj et al, also reported that 41% of T2DM patients in their study received monotherapy treatment. The selection of monotherapy versus polytherapy varies according to the BP levels and that makes prescribing pattern slightly different in different studies. Requirement of more than one antihypertensive agent suggest more severe form of HTN which needs adequate control.

We observed that antagonists of renin-angiotensin-aldosterone system were the most common drugs prescribed for control of HTN in patients. Following these, thiazide diuretics were second most frequently used agents.

Multiple studies have reported similar prescribing practices. Dhanraj et al, reported that ACEIs (59%) and ARBs (52%) were most frequently prescribed antihypertensives in their study from Punjab, India. A study from Jammu by Kaur S et al, reported ACEIs (33.8%) as most frequently prescribed drugs for control of HTN. Another study from Sharma JK et al, reported that ACEIs (85.36%) were the most common drugs for HTN treatment in T2DM. These studies suggest that ACEIs or ARBs remain the first-choice agent in HTN with T2DM. The JNC-8 guidelines also recommend these drugs as first choice agents in patients of HTN with T2DM. They have shown to provide end-organ protection and reduce the incidence of adverse cardiovascular outcomes and mortality in T2DM patients with HTN.

Among other choices of drugs, thiazide diuretics and beta-blockers were prescribed with nearly similar frequency and CCBs were used in lesser number of patients. However, a study from Dhanraj et al reported CCBs as second choice agents (29%) compared to diuretics (27%) or beta-blockers (14%). Contrast to this, Sharma et al. reported beta-blockers (33.44%) as second most frequently prescribed drugs followed by calcium channel blockers (29.95%). This suggest the choice of second drug might vary in different regions of India depending on the local practices and preferences of physicians and patients.

However, a lower use of CCBs in present study calls for action to improve their prescribing in HTN with T2DM as JNC-8 guidelines have recommended CCBs among the first-line agents than beta blockers. As far as individual therapies are concerned, there are no specific recommendations on individual molecules and can be preferred as per physician choices. Authors observed ramipril, telmisartan, hydrochlorothiazide, amlopidine and atenolol among the preferred drugs from their respective class.

As HTN and T2DM increase the risk of cardiovascular disease, preventive strategies are used in many of the patients. In supporting to this, authors observed prescription of antiplatelets and hypolipidemic drugs in 52.6% and 56.6% patients respectively.

This suggest that these individuals either had past CV event or might be at a higher risk of CV events qualifying for statin therapy as outlined in 2013 guidelines from American college of Cardiology and American heart association. Considering a long list of medication prescribed in patients T2DM with HTN, it is not unusual to observed 5 to 6 drugs per prescription authors observed that over half of the study patients had 5 to 7 drugs in one prescription.

Presence of comorbidities like CV disease, stroke, infections increase the number of drugs per prescription in such patients. Having more than 10 drugs in prescription of these patient points to the fact that their disease is not controlled well requiring multiple therapy. Therefore, this suggests that efforts are necessary to improve the control of hyperglycemia and hypertension in these patients.

CONCLUSION

In patients of HTN with T2DM, ACEIs/ARBS are most common drugs prescribed with most of them being monotherapy or dual drug therapy. Prescription of CCBs is on the lower side suggesting need to improve physician and patients’ awareness on possible benefits with these drugs compared to those of beta blockers. Concomitant use of statins and antiplatelet suggest preventive strategies are also undertaken in these patients who are at risk of CV disease. In all, the prescribing pattern of antihypertensives in patients of HTN with T2DM is rational and is as per guideline recommendations.
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