Letter to Editor Rheumatology
www.lettertoeditor.org

An international open-access and peer-reviewed online journal

Letter

Lett Ed Rheumatol
doi:10.2399/ler.12.0001

Treat to target (T2T) in rheumatoid arthritis – the con side

Eldad Ben-Chetrit, MD

Rheumatology Unit, Hadassah - Hebrew University Medical Center, Jerusalem, Israel

Abstract

The "treat to target" (T2T) approach, aiming to manage rheumatoid arthritis (RA) more tightly, is becoming rather popular. This idea was derived from the therapeutic approach used in conditions such as diabetes mellitus (DM), hypertension (HTN) and dyslipidemia. The idea is well taken but there are important caveats which mainly stem from the fact that there are fundamental differences between RA, DM, HTN and dyslipidemia. The same holds true for the medications that we use to manage RA versus the medications used in the other listed conditions.

Key words: Rheumatoid arthritis, treatment, tight control.

Dear Editor,

The "treat to target" (T2T) approach in managing (RA) is becoming rather popular.[1] This idea aiming to control RA more tightly, was derived from the therapeutic approach used in diabetes mellitus (DM), hypertension (HTN) and dyslipidemia. It has been shown that tight control of these medical conditions resulted in better outcomes.[2-8] The T2T recommendations for RA include following the patient closely and considering alterations in treatment every 1-3 months if necessary in order to receive a complete remisson.[9,10]

The idea is well intentioned however there are important caveats which mainly stem from the fact that there are fundamental differences between RA, DM, HTN and dyslipidemia. The same holds true for the medications we use to manage RA versus the medications used in the other listed conditions. to treat these compared to RA.

1. Evaluation of the effect of treatment. In DM, HTN or dyslipidemia there is a single dominant parameter – glucose, blood pressure or cholesterol levels – to assess a treatment response. This is not so for RA.

2. Systemic manifestations of RA. RA presents mainly by joint involvement but it is also a systemic disease with fever, night sweats, weight loss and heart or lung involvement. In these cases, how should we define remission if the main clinical problem is systemic rather than arthritic? In DM, HTN or dyslipidemia the parameter for evaluation is seldom systemic.

3. Drug characteristics – immediate versus late effects. The medications we use in treating DM, HTN and dyslipidemia, have an effect on the main disease parameter (i.e blood glucose) we can observe usually rather rapidly, even within minutes. On the other hand sometimes one needs to wait several months in order to appreciate the effect of the medications for RA. Thus, the recommendation to consider changing medications within 1-3 months may not be applicable in RA. Plenty of data suggests response in up to 30% of patients 3-6 months after treatment.

4. Drug characteristics – chemicals versus biologics – predictability of their effect. The medications for controlling DM, HTN or dyslipidemia are chemical molecules produced synthetically, allowing a precise evaluation of their effect. In RA, the main effective treatments are "biologic agents" which are produced by cells and affect biological pathways. Thus the efficacy of a biologic substance may be difficult

***Correspondence:**
Eldad Ben-Chetrit, MD
Rheumatology Unit,
Hadassah - Hebrew University Medical Center Jerusalem, Israel
e-mail: Eldad@hadassah.org.il

Citation: Ben-Chetrit E. Treat to target (T2T) in rheumatoid arthritis – the con side. Lett Ed Rheumatol 2012;2:e120001. doi:10.2399/ler.12.0001

Received: January 3, 2012; **Accepted:** January 12, 2012; **Published:** January 18, 2012

Conflicts of Interest: The author has declared that no conflicts of interests exist.

to measure or estimate compared with the synthetic agents. Moreover, it may well be that changing the treatment will result in non response or even worsening the medical condition rather than improving it – a case which does not occur when treating DM or HTN. Thus there are many unexpected variables in using the "biologic agents" which are related to the medication itself, the patients and the characteristics of their disease.

5. Tight control proved to be perhaps not very desirable in DM and HTN. Last but not least, recent studies concerning our enthusiastic approach in tightly controlling glucose levels, blood pressure or serum cholesterol resulted in poor outcomes with higher rates of mortality due to hypoglycemic episodes and severe hypotension.[11,12] Similarly in RA we do not yet know what will be the cost of tight control of the joint disease in the long term outcome regarding complications such as infections or malignancies. It may well be that the current positive outcome of treatment with biologic agents is a result of their administration after serious and careful consideration and in the appropriate dosage. Pushing them to higher dose or more frequent changes in order to achieve a better target may increase the risk at long term.

In summary in assessing the T2T approach for widespread use, we should not forget that the analogy to other chronic diseases such as DM, HTN or dyslipidemia is not quite satisfactory. As a matter of fact, the first "Swallow", a paper supporting the above caveats has just been published.[13]

References

1. Schoels M, Knevel R, Aletaha D, et al. Evidence for treating rheumatoid arthritis to target: results of a systematic literature search. *Ann Rheum Dis* 2010;69:638-43.
2. Staessen JA, Wang JG, Thijs L. Cardiovascular protection and blood pressure reduction: a meta-analysis. *Lancet* 2001;358:1305-15.
3. Cannon CP. The IDEAL cholesterol: lower is better. *JAMA* 2005; 294:2492-4.
4. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329:977-86.
5. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998;352:837-53.
6. Rydén L, Standl E, Bartnik M, et al. Guidelines on diabetes, prediabetes, and cardiovascular diseases: executive summary. Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2007;28:88-136.
7. Action to Control Cardiovascular Risk in Diabetes Study Group; Gerstein HC, Miller ME, Byington RP, et al. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 2008;358:2545-59.
8. Currie CJ, Peters JR, Tynan A, et al. Survival as a function of HbA(1c) in people with type 2 diabetes: a retrospective cohort study. *Lancet* 2010;375:481-9.
9. Smolen JS, Aletaha D, Bijlsma JWJ, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis* 2010;69:631-7.
10. Schoels M, Knevel R, Aletaha D, et al. Evidence for treating rheumatoid arthritis to target: results of a systematic literature research. *Ann Rheum Dis* 2010;69:638-43.
11. ACCORD Study Group; Gerstein HC, Miller ME, Genuth S, et al. Long-term effects of intensive glucose lowering on cardiovascular outcomes. *N Engl J Med* 2011;364:818-28.
12. Cooper-DeHoff RM, Gong Y, Handberg EM, et al. Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary artery disease. *JAMA* 2010; 304:61-8.
13. van Eijk IC, Nielen MM, van der Horst-Bruinsma I, et al. Aggressive therapy in patients with early arthritis results in similar outcome compared with conventional care: the STREAM randomized trial. Rheumatology (Oxford). 2011 Dec 13. [Epub ahead of print]

