Invited Comment

Duration of dialysis sessions—was Hegel right?

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‘What history teaches is this: that people have never learned anything from history or acted on principles deduced from it’

Hegel G. Introduction in Philosophy and History (1832)

The history of dialysis teaches us that a reduction in dialysis time in the USA was accompanied by a reduction in life-expectancy

In the 1980s, a surprising result was highlighted by a number of studies evaluating the survival of haemodialysis patients in different countries: European and Japanese ESRD patients had a better survival than those treated in the USA [1,2]. In 1993 the expected remaining lifetime for dialysis patients aged 45–65 years was three times higher in Japan than in the USA. Some caution was required when making the comparison because the standardized mortality ratio methods used adjust only for age, gender, race, and the cause of end-stage renal disease (and not for comorbidities), but the importance of these data prompted a provocative editorial by Nōsé [3] entitled ‘Why do we kill so many patients on hemodialysis in the USA?’ The author’s conclusion was that USA patients were underevaluated because the substantially inadequate reimbursement of haemodialysis procedures in the USA made it almost impossible to provide sufficient dialysis therapies to patients. An analysis of the dialysis prescriptions made in 1986 and 1987 [4] found that the prescribed level of dialysis in the USA was substantially lower than in Europe; furthermore, the most striking feature of these lower haemodialysis dose was the progressive decrease in the duration of dialysis sessions, which were 23.5% shorter than in Europe and 40% shorter than in Japan (where the reimbursement was proportional to the duration of dialysis).

Are the Japanese going to forget the lesson of history?

In an equally provocative editorial entitled ‘Don’t kill Japanese hemodialysis patients like America kills its patients’ [5], Nōsé has expressed his fear that Japanese dialysis centres will soon follow the example of their American counterparts. He warned Japanese practitioners to maintain good haemodialysis procedures despite the actual reimbursement crisis in Japan.

Are Lombardy nephrologists going to make the same mistake?

The EDTA estimates may not be perfectly reliable because of the low reply rate. In contrast all of the 44 dialysis centres in Lombardy regularly supply data. Looking at the 1983–1996 data of the Lombardy Registry of Dialysis and Transplantation [6] the decrease in dialysis time stands out a mile: the number of dialysis sessions lasting less than 3 h (three times/week) has increased from 4 to 16.3%, the number of those lasting 3–4 h has increased from 55.4 to 71.6%, and the number of those lasting 4–5 h has decreased from 39.9 to 11.8%. However, the survival of Lombardy patients is still better in comparison with those treated in the USA, even after adjustment for comorbidities [7,8].

At a time when the USA has shown that it is well aware of the risks of reducing treatment time and has begun to reverse the trend of the eighties which clearly reduced standardized mortality ratio over recent years [9], and when Japanese are warned not to make the same mistake as the Americans did in the past, Lombardy seems to be going into the opposite direction apparently without having any qualms. If we refute the statement of Hegel and assume that history can teach us to avoid repeating dangerous mistakes, we feel that this is the time for nephrologists in Lombardy (and Europe) to reconsider the issue of duration of dialysis sessions. The best incentive to raise this point is the observation of Charras et al. [10] that patients treated with ‘long’ dialysis have the best survival (75% at 10 years).
The history of short dialysis

The widespread trend towards shortening the duration of dialysis sessions has been driven by a number of factors (the cost/effectiveness ratio, patient—staff convenience, improved technology), but its justification is founded on the evolution of scientific knowledge. The introduction of the concept of the square meter hour hypothesis in 1971 [11] suggested that dialysis time (the only dialytic parameter that entirely depends on prescription) could be shortened with impunity as long as the dialyser surface area was increased to yield the same surface area \( \times \) time product.

The concept of dialysis quantification (Kt/V)

In 1983 Gotch and Sargent [12] introduced the parameter Kt/V for urea as a predictor of patient outcomes, and this has had an even more important effect on the prescription of the duration of dialysis sessions. This was due to the results of a re-analysis of the data provided by the National Cooperative Dialysis Study (NCDS) [13], the only large-scale prospective study designed to compare patient outcomes after short and long treatment sessions based on different TAC urea. Although the correlation between outcome and treatment time only showed a non-significant trend (\( P = 0.06 \)), there was a close correlation between patient outcomes and Kt/V, which was therefore assumed to be the best means of estimating dialysis adequacy. Given that there was no difference in the way that Kt/V of more than 1.0 was reached, it was assumed that the value of \( t \) could be safely reduced provided that K was increased in order to maintain the K \( \times \) t product constant.

What does adequacy of dialysis actually mean?

Analysis of the NCDS data clearly shows that a low Kt/V ratio also means an inadequate correction of acidosis and electrolyte derangement. Furthermore, the reappraisal of data published by Keshaviah [14] suggests a curvilinear relationship between Kt/V and morbidity. Finally, the impressive results obtained by Charra et al. [10] with very long dialysis sessions (8 h) raise serious doubts about the validity of the assertion that lower morbidity and mortality rates correlate with higher haemodialytic doses. This correlation has been clearly confirmed by a historical prospective study [16], controlled for a long list of comorbid conditions, of a randomly selected national sample of over 2300 Medicare ESRD patients. However, in this analysis, the prescribed treatment time did not significantly correlate with the risk of mortality despite the large sample size and adjustments for comorbid conditions and other covariates, and there was not even a suggestion that a longer treatment time (at the same Kt/V) provides any benefit in terms of survival. Furthermore, the considered treatment times were those prescribed, which may not always match delivered treatment time. A possible explanation for this could be that the prescribed dialysis treatments covered a narrow range of 3–4 h; no conclusion can therefore be drawn from these data concerning the possible benefit of 5–8 h treatments (the times used in Tassin [10]). Consequently, there are currently no conclusive results making it possible to establish whether, for a given value of Kt/V, high clearance and a short treatment time is worse or better than low clearance and a long treatment time. The only thing that we know for certain is that the risk of mortality inversely correlates with the delivered dialysis dose.

How can the Japanese and Tassin data be reconciled with those showing no treatment time effect?

The excellent survival results reported in Japan [1] and by Charra et al. [10] do not conflict with an inverse correlation between mortality and dose: the smaller size of the Japanese population means that longer treatment time is the equivalent of a higher dialysis dose, and the Kt/V reported by Charra in his patients averaged 1.7.

Moreover, since efficiency can vary greatly, treatment time is now a meaningless expression of treatment quantity. The ability to increase the solute removal rate has created a conceptual difference between treatment time and treatment ‘dose’. A short treatment time is no longer synonymous with less therapy, and long treatment sessions do not necessarily imply more solute removal. However, it is very likely to be so in everyday clinical practice.

Treatment time per se cannot replace the quantification of dialysis adequacy

It cannot be assumed that treatment time—especially if empirically defined—can replace Kt/V or, more generally, urea kinetics as an index of dialysis adequacy. This is particularly true if the dialysis is quantified on-line without blood and dialysate sampling, and at no extra cost [17]. The problem in prescribing and delivering an adequate dialytic treatment lies in the correct application of dialysis quantification which, to be successful in clinical practice, requires a comprehensive approach that acknowledges
the underlying clinical principles and technical aspects, a team of skilled and motivated nurses and physicians, and motivated and compliant patients.

Optimal vs adequate dialysis

Central to the evaluation of dialysis adequacy is a definition of adequate \( Kt/V \), but this is still something of an open question. It is certainly fair to say that today’s consensus is that 1.2 is the minimum adequate value of \( Kt/V \). Accepting this value as a definition of adequate dialysis, and bearing in mind that shortening dialysis time requires an increase in the rate of solute removal in order to maintain a constant \( Kt/V \) value, we can try to define the minimum treatment time for delivering this dialysis dose, which of course will depend on dialysate urea clearance, the body weight of the patient, the operational conditions and last, but not least, the possibility of reaching dry body weight. Moreover, the removal of middle molecules is dependent on treatment time but, even more importantly, on the type of membrane.

Time as a safety factor: the shorter the time, the greater the risks

What must be stressed is that the impact of a number of possible risks is greater, the shorter the treatment time. Because of common errors in applying urea kinetic modeling, it is very likely that the prescribed time is often unappropriately short to attain the target \( Kt/V \) and dry body weight. Furthermore, there is often a difference (and sometimes a large difference) between prescribed and delivered dialysis but, because delivered dialysis is not routinely verified [17], underdialysis may go unnoticed and thus have deleterious clinical effects in the long term. This risk is the greater the shorter is the prescribed treatment time. Obviously, a shorter treatment time reduces the ‘reserve dose’ that can compensate for the operational imperfections of dialysis. It is evident that only a prescribed dialysis duration exceeding the minimum defined from a theoretical point of view allows some protection from the risk of dangerously inadequate treatments.

Treatment time per se and blood-pressure control

The clinical results reported by Charra et al. [10] underline the importance of treatment time in relation to an additional aspect of dialysis adequacy (besides depurative adequacy): achieving dry body weight and thus normalizing blood pressure. Cardiovascular mortality accounts for approximately 50% of the mortality of dialysis patients, and hypertension is the main cause of cardiovascular morbidity and mortality; on the other side around, intradialytic hypotension is the main acute complication of haemodialysis. Blood pressure control in patients on chronic haemodialysis basically depends on the maintenance of normal or near-normal extracellular volumes [18]. If dialysis fails to ensure adequate salt and water removal, hypertension will usually persist despite the use of antihypertensive medication. Longer dialysis sessions make it possible to avoid the high hourly ultrafiltration rates that often cause severe hypotensive episodes that prevent the attainment of dry body weight.

The lesson of history and the progress of knowledge

In conclusion, although target \( Kt/V \) can be obtained by means of greater dialytic efficiency and/or a longer dialysis time, most of the symptoms experienced by patients during haemodialysis are related to their poor tolerance of fluid removal. Prolonging dialysis time makes fluid removal easier and thus not only makes it possible to reach dry body weight and control blood pressure, but also allows better correction of electrolyte and acid—base imbalance. Treatment time therefore cannot be reduced to below the point at which fluid removal is associated with an unacceptable increase in symptoms. Today, the onset of symptoms while removing interdialytic weight gain is the limiting factor in reducing treatment time. Because of this relationship the search for more efficient dialysers and dialysing techniques is futile.

The main lesson of history seems to be that, in order to prescribe an adequate dialytic treatment, sufficient emphasis must be put on the duration of dialysis per se, because this factor determines whether dry body weight can be attained, blood pressure be controlled, and cardiovascular morbidity and mortality be reduced. On the other hand, one must avoid the risk of oversimplification: if we act on a purely empirical basis, we may lose improvements derived from the progress of knowledge. History teaches us to avoid repeating the mistakes of the past, but also to keep an open mind when true progress occurs.

But at the end we hope that the current most unfortunate trend to shorten the duration of dialysis sessions in Lombardy will not continue in view of the ample demonstration in the past that short dialysis sessions are disadvantageous.

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