Routine Testing not Beneficial in Evaluation of Patients with Chronic Spontaneous Urticaria

Dear Editor,

We read with interest the paper by Shailaja Chauhan and colleagues where they found that elevated plasma levels of D-dimer in patients with chronic spontaneous urticaria (CSU) may influence treatment options,[1] but the tests did not make any difference in the overall management of patients. We present our experience with a quality improvement project, which determined the usefulness of routine testing in CSU. The British Society of Allergy & Clinical Immunology guidelines[2] were used as standards [Table 1] and was approved by the Clinical Audit and Effectiveness Team of Hull University Teaching Hospitals NHS Trust. Patients with CSU were identified from clinic letters. The first phase (Plan, Do, Study Act Cycle 1) reviewed 169 new consultations for 7 months between September 2018 and March 2019, with a follow-up phase (PDSA Cycle 2) of 190 new consultations for 4 months between September 2019 and December 2019. Performances with regards to standards are shown in Table 1.

A total of 763 blood tests were done on 44 patients (34 females; mean age 42.6 years with age range 17-83 years) in the first phase of the project. Of these, 12 were abnormal but only 2 (0.3%) results led to a change in the management (IgG lambda paraprotein, thyroiditis with undetectable thyroid-stimulating hormone (TSH)) [Figure 1]. 93 specific IgE tests were done and 14 patients underwent further skin tests of which 71% of skin tests were either dermographic or negative. The positive specific IgE tests were to aero-allergens such as house dust mite or animal dander that were identified on skin tests but patients felt that this was not new information, or changed the way CSU was managed. In total, 84% of patients had 25-hydroxy-vitamin D3 levels tested, and 87% of patients had vitamin B12, folate and ferritin levels tested. The total cost of evaluating patients with urticaria (excluding complement C3, C4, and C1-inhibitor tests) was at least $2400 (equivalent to INR 1,80,000). Based on the findings of PDSA Cycle 1, the Directory of Services (DoS) for Immunology was revised and a pathway for referral into secondary care was published. The investigations that could be requested at CSU evaluation were changed to include: full blood count, biochemistry profile, thyroid function (TSH, fT4 if on thyroid medication), tryptase with complement C3 and C4 testing reserved only for patients with angioedema.

The second phase (PDSA Cycle 2) identified 30 patients (22 females; mean age 40.9 years with range 16-92 years) with chronic spontaneous urticaria and angioedema where a total of 262 tests were done (including 73 specific IgE tests). Of these, 21 results were abnormal and only one (0.4%) altered management (positive specific IgE to ω-5-gliadin) [Figure 1]. No skin prick testing, 25-hydroxy-VitaminD3 levels or hematinics (folate, ferritin, vitamin B12) were requested in this cycle. The positive specific IgE results were against aero-allergens (dust mites, animal dander, pollens) similar to what was identified in the first phase, and did not influence management other than

Table 1: Standards used for the quality improvement project with results

Standards	Information audited from clinic letters	Failure of audit	Required to pass the audit	1st phase results (*n*=44)	2nd phase results (*n*=30)
Standard 1: Quality of history taking	Red, itchy wheals lasting less or >6 weeks; any obvious triggers (drugs, foods, etc); skin lesions lasting >24 h with bruising; physical stimuli identified; any features of anaphylaxis	None recorded	3 of 5 recorded in letters/case notes	100%	93%
Standard 2: Testing criteria	Clinical features consistent with a trigger to warrant specific IgE or skin tests; full blood count, biochemistry profile, thyroid function; autoantibody tests or other special tests such as H. pylori testing should be justified	Overtesting if specific IgE and skin tests were requested with no clear clinical triggers	Adequate information on letter to justify tests	68%	93%
Standard 3: Communication	Patient and referral physician should be provided with adequate information on diagnosis and management options in the community	No information leaflet provided to patient; no clear management plan	2 of 2	86%	100%
Standard 4: Safety	Adequate information and training provided to patient if there were any features suggestive of anaphylaxis especially if adrenaline auto-injectors were prescribed	None recorded after prescribing; patient not trained with use of device	Training must be provided	100%	100%

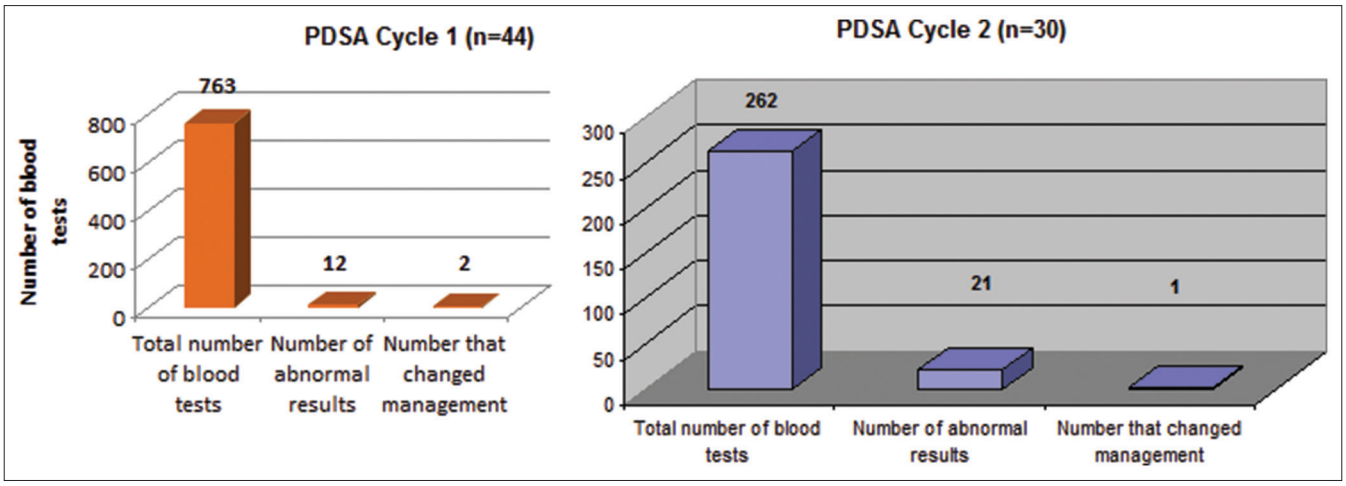

Figure 1: Routine tests in patients with chronic spontaneous urticaria have limited utility. The first phase showed only 2 (0.3%) of 763 tests made a change in overall management indicating an excess of tests were being requested. While there was an improvement in the numbers of tests requested in the second phase, still only 1 (0.4%) of 262 tests influenced clinical management

helping patients realize management of underlying atopy/environmental allergies will help control the urticaria. The total cost of evaluating patients in the second phase was at least $800 (equivalent to INR 60,000), accounting for tests done in the majority of patients. There was an improvement in 28% points that met the standards.

In conclusion, there was no evidence that routine testing in the evaluation of CSU made any change in treatment or that patient safety is likely to be compromised if no tests were offered, if the clinical history was accurate. Although the DoS allowed minimum tests that could be offered, it had a less than expected effect on the way testing was recommended. Our findings are consistent with that of Carrillo-Martin I *et al*.[3] where only 0.9% of patients (5 of 725 patients) had a change in outcome with routine testing and $569 were spent in evaluation, management, and costs of tests. However, we agree that it is completely acceptable to request blood tests as per clinical need such as an antinuclear antibody (when the urticaria presents with features of connective tissue disease such as joint pains, photosensitive skin rash, etc), C-reactive protein or serum electrophoresis or skin biopsy (features of autoinflammation such as Schnitzler syndrome), thyroid autoantibodies (if there is a strong family history of autoimmune thyroid disease), including special tests where specific centers have the facility to perform an autologous serum skin test or the basophil CD63/CD203c expression tests.[4-6]

We feel that the reasons for testing patients are probably influenced by multiple factors such as (1) pressure on physicians to ensure that there are no secondary triggers; (2) negative allergy results may decrease anxiety; (3) conflicting opinions of physicians about 'triggers'; and (4) tendency to generalize reports that have identified some biomarkers in certain types of CSU. We hope this additional data will be of value in convincing caregivers that routine testing in patients with CSU is of low benefit and only adds to the ongoing costs of therapy.

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Conflicts of interest

There are no conflicts of interest.

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