Gastroenteritis and infection markers: Significant increase of C-reactive protein in salmonellosis

Gastroenteritis und Infektionsmarker: Signifikante Erhöhung von C-reaktivem Protein bei Salmonellose

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Summary

In the University Children's Hospital of Frankfurt/Main, 331 patients with diarrhoea were examined retrospectively for the infection markers CRP, leucocyte count (LC) and ESR. Out of these, 62 had salmonellosis, partly with mixed gastrointestinal infection (n = 25) and/or combined with other disease. Twenty-five of these had salmonellosis only. These were compared either with a *Rotavirus* group (n = 29, group 1), which was the second most common form of enteritis, or with a total group including all non-*Salmonella* infections (n = 39, group 2). In this investigation, 88 % of the patients with Salmonella enteritis had increased CRP values (mean: 6.35 mg/dl). A significant increase ($p < 0.0001$) in CRP was found even on the first day after hospitalization. Combined with the symptom diarrhoea, CRP alone discriminates between salmonellosis and *Rotavirus* infection with a sensitivity of 0.88 and specificity of 0.86. The sensitivity and specificity in the discrimination between salmonellosis and all other gastrointestinal infections was 0.88 and 0.79 respectively. In a discriminant analysis between CRP, LC and ESR in the 3 different groups, the LC and/or the ESR revealed no additional diagnostic significance than CRP alone. *Shigella* (n = 2) and *Lamblia* (n=1) enteritis are rare infections of minor importance in this context. Early detection of salmonellosis enhances the possibility for improved medical care.

Key words

Salmonellosis – C-reactive protein – leucocyte count – erythrocyte sedimentation rate – gastroenteritis – infection marker

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Zusammenfassung

Am Zentrum der Kinderheilkunde, Universitätskliniken Frankfurt/Main wurden 331 Patienten mit Diarrhoe retrospektiv auf die Infektionsmarker CRP, Leukozytenzahl (LC) und BSG untersucht. Von diesen hatten 62 Salmonellose, teilweise mit einer gastrointestinalen Mischinfektion (n = 25) und/oder kombiniert mit einer anderen Erkrankung. Eine Gruppe von 25 Patienten hatte ausschließlich Salmonellose. Diese Patienten wurden entweder mit einer Gruppe (n = 29) mit *Rotavirus*-Enteritis (der zweithäufigsten Enteritis-Form, Gruppe 1), oder mit einer Gesamtgruppe, bestehend aus allen nicht-*Salmonella* Infektionen (n = 39, Gruppe 2), verglichen. Die zwei letztgenannten Gruppen waren ebenfalls diagnostisch homogen. Dabei hatten 88 % der Patienten mit Salmonellose erhöhte CRP-Werte mit einem Mittelwert von 6,35 mg/dl. Eine signifikante CRP-Erhöhung ($p < 0,0001$) war schon am ersten Tag der stationären Aufnahme feststellbar. Beim Leitsymptom Diarrhoe unterscheidet die CRP-Bestimmung zwischen Salmonellose und *Rotavirus*-Enteritis mit einer Sensitivität von 0,88 und einer Spezifität von 0,86. Die Sensitivität und die Spezifität bei Vergleich zwischen Salmonellose und Gruppe 2 waren 0,88 bzw. 0,79. *Shigella*- (n = 2) und *Lamblia*-Enteritis (n = 1) sind relativ selten und haben in diesem Zusammenhang eine entsprechend geringe praktische Bedeutung. In einer Diskriminanzanalyse zwischen CRP, LC und BSG in den 3 verschiedenen Gruppen ergaben die LC und die BSG keine zusätzliche diagnostische Aussage zu der ausschließlichen Bewertung von CRP. Ein frühzeitiger Hinweis auf *Salmonella*-Enteritis bedeutet verbesserte Möglichkeiten in der medizinischen Versorgung.

Schlüsselwörter

Salmonellose – C-reaktives Protein – Leukozytenzahl – Blutsenkungsgeschwindigkeit – Gastroenteritis – Infektionsmarker

Introduction

Salmonellosis is a relatively common, severe infection in several countries [1–3]. The number of infections has rap-

idly increased over the last years [3] and the cost of medical care due to an epidemiological outbreak is rapidly growing [2, 4, 5]. *Salmonella* (S.) infection is frequently found in AIDS [6–7]. The pathophysiological mechanism of *Salmonella*-induced enteritis is poorly understood [8]. A specific and sensitive parameter for the early evidence of *Salmonella* enteritis is of practical importance, since bacteriological data are first available after several days and outbreaks in clinical wards are difficult to control [9].

An increase in serum CRP, produced in the liver in the acute phase, has been observed in different forms of infections, particularly those of severe bacterial origin [10].

The aim of the present investigation was to evaluate pathological laboratory test-results in different forms of enteritis.

Materials, Methods and Patients

CRP determinations were performed by nephelometry (Sanofi Diagnostics Pasteur on a Kallestad QM 300 nephelometer) with original reagents from the same firm. The precision of this method was good (typically CV in day-to-day evaluations: 5.8 %; within-run: 2.4 %). The reference range for CRP in our laboratory is < 1.2 mg/dl. ESR measurements were performed with the Westergren method (normal values 0 – 10 mm/h) and LC either on a Du Pont Cell-Dyn 1600 counter or manually. The distribution of age-dependent normal values for the latter methods is in accordance with those published by Hathaway and co-workers [9].

Patients with salmonellosis and other forms of enteritis/gastroenteritis were investigated retrospectively for pathological laboratory results during the last five years. Those with a duration of disease of more than 14 days before hospitalization and patients with more than one diagnosis were excluded from this investigation. The age of the patients was between newborn and nine years. Statistical determinations of P values were performed two-sided with the Mann-Whitney test.

Bacteriological/virological examinations revealed the following for the Salmonella-group: *S. enteritidis* (n = 15); *S. typhimurium* (n = 6); *S. virchowi* (n = 1); *S. infantis* (n = 1); *S. parathyphi B* (n = 1); *S. typhi* (n = 1), other findings: *Rotavirus* (n = 29); *Shigella boydii* (n = 1); *Shigella sonnei* (n = 1); *Escherichia coli 1* (n = 1); *Lamblia intestinalis* (n = 1); *Candida* (n = 6) and mixed gastrointestinal infections: *Salmonella/Rotavirus* (n = 11), *Salmonella/Candida* (n = 14) and *Rotavirus/Candida* (n = 25).

Abbreviations:
CRP = C-reactive protein
ESR = erythrocyte sedimentation rate
LC = leucocyte count

Results

In the comparison of the *Salmonella* group with group 1, a significant difference ($p < 0.0001$) in serum CRP levels was observed. With the exception of three patients, the *Salmonella* group had serum CRP values of 1.2 mg/dl or higher with a range up to 21.3 mg/dl and a mean of 5.7 mg/dl. One of the highest values (20.3 mg/dl) was found in typhoid fever. One *Salmonella* patient was examined for CRP on the 14th day after disease onset and was found normal (0.6 mg/dl). On the 1st day of hospitalization ($n = 15$) a significant CRP increase ($p < 0.0001$) was found with a range between 1.4 and 21.3 mg/dl and a mean of 6.58 mg/dl. One of the latter patients had a normal CRP value (< 0.5 mg/dl). In group 1, four and in group 2, eight patients had increased CRP values, demonstrated in tables 1, 2. In salmonellosis ESR was increased in 19 examinations, but with a great number of false positive results and a corresponding poor specificity. The LC in the *Salmonella* group and in group 1 and 2 was elevated in 8 patients out of 22, in 5 out of 28 and in 12 out of 37 patients, respectively. In table 1 – 4 the diagnostic characteristics [11] of these results are demonstrated. In a discriminant analysis, including the three parameters and the three groups, the highest percentage of correctly classified grouped cases was obtained for CRP alone (74.1 % in comparison 1 and 70.3 % in comparison 2).

It is apparent that the LC sensitivity and the ESR specificity are both insufficient for diagnostic purposes. A slight, temporary leucopenia was observed in the patient with typhoid fever, in 2 patients with S. enteritidis and in 1 Patient with *Rotavirus* infection (not demonstrated).

The distribution of CRP results in gastrointestinal infections is shown in Table 5. In Fig. 1 the CRP elevation in a patient with salmonellosis is demonstrated.

Table 1. Distribution of positive and negative results.

	Salmonellosis / Group 1			
Parameter	True pos.	False pos.	True neg.	False neg.
CRP	22	4	25	3
LC	8	5	23	14
ESR	19	5	2	2

Table 2. Distribution of positive and negative results.

	Salmonellosis / Group 2			
Parameter	True pos.	False pos.	True neg.	False neg.
CRP	22	8	31	3
LC	8	12	25	14
ESR	19	11	4	2

Table 3. Diagnostic characteristics

Salmonellosis / Group 1			
Evaluation	CRP	LC	ESR
Sensitivity	0.88	0.36	0.90
Specificity	0.86	0.82	0.29
PV +	0.85	0.62	0.79
PV -	0.89	0.62	0.50

PV + = predictive value positive,
PV - = predictive value negative.

Table 4. Diagnostic characteristics

Salmonellosis / Group 2			
Evaluation	CRP	LC	ESR
Sensitivity	0.88	0.36	0.90
Specificity	0.79	0.68	0.27
PV +	0.73	0.40	0.63
PV -	0.91	0.64	0.67

PV + = predictive value positive,
PV - = predictive value negative.

Table 5. CRP elevation in different forms of gastroenteritis.

Infection	total n	CRP elevation n	mean CRP* mg/dl	SD
Salmonellosis	25	22	6.22	5.85
Rotavirus	29	4	3.72	8.82
Shigella	2	2	11.45	11.45
Lamblia	1	1	2.95	–
Coli	1	0	–	–
Candida	6	1	7.90	–

* = maximum value from each patient.

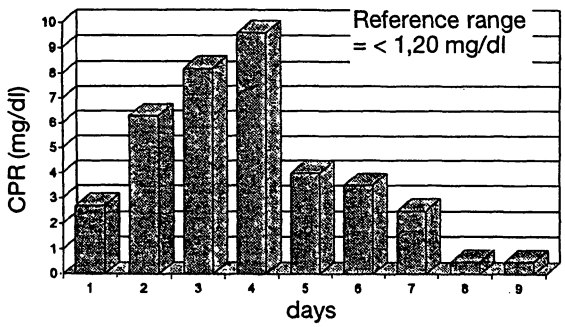

Fig. 1. CRP elevation in a patient with salmonellosis (*Salmonella typhimurium* infection).

Discussion

The diagnostic characteristics of CRP in gastrointestinal infections discriminate reliably to form basis for therapeutic and epidemiologic management decisions, in particular to prevent outbreakes in clinical wards. For the diagnosis of *Salmonella* infection the bacteriologic examination is time-consuming (days), whereas a quantitative CRP-result is available as an emergency test within minutes. Because of the high frequency of *Salmonella* and *Rotavirus* infections, this is an important finding for following reasons: by positive stool screening-test for *Rotavirus* (which is rapid and specific), aditional information about a possible mixed infection with *Salmonella* can be given by CRP elevation; a negative *Rotavirus* test combined with CRP-elavation, will differentiate between Salmonellosis and a great number of unspecific (bacteriologic/virologic negative) gastrointestinal diseases with similar symptoms; a very high CRP value observed in typhoid fever indicates that CRP values above a certain thresold may be useful for deciding antibiotic therapy before bacteriological results are available, but this remains speculative until further investigations have been conducted.

Patients with *Shigella* (n = 2) and with *Lamblia* enteritis (n = 1) were also shown to have increased CRP values. The latter findings are of minor importance, since these infections are rare.

An initial CRP screening of all patients with the clinical symptom diarrhoea represents an easy, powerful and well-aimed diagnostic tool which will be useful in preventing outbreaks and improving the treatment of salmonellosis. We assume that this will also be true for typhoid and paratyphoid fever.

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References

1. Chalker RB, Blaser MJ (1988) A review of human salmonellosis: III. Magnitude of salmonella infection in the United States. Rev Infect Dis 10, 111–124
2. Hayes C, Lyons RA, Warde C (1991) A large outbreak of salmonellosis and its economic cost. Ir. Med. J. 84, 65–66.
3. Desgrandchamps D, Altwegg M, (1990) Salmonellen-Gastroenteritis: Ursachen, Folgen, therapeutische Perspektiven. Schweiz Med Wschr 120, 1751–175
4. Roberts T (1988) Salmonellosis control: estimated economic costs. Poult Sci 67, 936–43
5. Roberts JA, Sockett PN, Gill ON (1989) Economic impact of a nationwide outbreak of salmonellosis: cost-benefit of early intervention. B M J 298, 1227–1230

6. Sperber SJ, Schleupner CJ (1987) Salmonellosis during infection with human immunodeficiency virus. Rev Infect Dis 9, 925–934
7. Tocalli L, Nardi G, Mammino A, Salvaggio A, Salvaggio L (1991) Salmonellosis diagnosed by the laboratory of the 'L. Sacco' Hospital of Milan (Italy) in patients with HIV disease. Eur J Epidemiol 7, 690–695
8. Stephen J, Wallis TS, Starkey WG, Candy DC, Osborne MP, Haddon S (1985) Salmonellosis: in retrospect and prospect. Ciba Found Symp 112, 175–192
9. Hathaway WE, Hay WW Jr, Groothiuis JW, Paisley JW, (eds.) (1993) Pediatric Diagnosis & Treatment. Appleton & Lange: Prentice-Hall Internat, pp 1033–1034
10. Young Barbara, Gleeson Maree, Cripps AW (1991) C-reactive protein: A critical review. Pathology 23 118–124.
11. Schwartz JS, (1987) Understanding of laboratory results. Med Clin N Amer 71, 639–652