

Factors Affecting Bilirubin Levels Following Drainage Procedures in Obstructive Jaundice

Tıkanma Sarılığında Drenaj İşlemleri Sonrası Bilirubin Düzeylerini Etkileyen Faktörler

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Öz

Giriş: Serum bilirubin seviyelerinin ölçülmesi oldukça kolaydır ve neredeyse her sağlık kurumunda halihazırda bulunur. Pratikte hekimler tarafından obstrüktif sarılık hastalarının takibinde kullanılır. Takip için bir belirteç olarak yaygın kullanımına rağmen, bu klinik belirtinin klinik olarak yorumlanması hakkında literatür net verilerden yoksundur. Özellikle biliyer drenaj prosedürlerini takiben bilirubin azalmasıyla ilgili açıkça belirlenmiş prognostik kurallar ve limit noktaları bulunmamakta olup özellikle bilirubin azalma hızına etki eden faktörler tartışmalıdır. Tıkaçıcı sarılığın girişimsel drenajını takiben bilirubin düzeylerini etkileyen olası faktörleri belirlemek için bir başlangıç noktası oluşturmak amacıyla retrospektif bir çalışma yaptık.

Gereç-Yöntem: Üçüncü basamak sağlık kuruluşunda 4 yıllık bir süre boyunca girişimsel drenaj prosedürleri uygulanan 73 tıkanma sarılığı hastasına ait verileri retrospektif olarak inceledik.

Bulgular: Drenajı takiben bilirubin seviyesindeki düşüş en hızlı olarak ilk 48 saat içinde şekilde gerçekleşti. Analiz edilen değişkenlerden sadece yaş ve seçilen drenaj prosedürü tipi hasta grubumuzda bilirubin düşüşü oranını anlamlı derecede etkiledi. Yavaş bilirubin azalması olan hastaları doğru bir şekilde tahmin edebilecek limit noktaları ise elde edilemedi.

Sonuç: Serum bilirubin düzeyi, tıkanma sarılığı olan hastalarda tedavi başarısını ve hasta prognozunu öngören önemli ve yaygın kullanılan bir belirteçtir .Drenaj tipi ve yaş, altta yatan patolojiden bağımsız olarak, bilirubin azalmasını etkilemektedir.

Anahtar Kelimeler: Bilirubin, drenaj, tıkanma sarılığı

Abstract

Introduction: Measuring serum bilirubin levels is easy and readily available in virtually every healthcare facility. It is practically used by physicians for the follow up of the patients with obstructive jaundice.Despite its common use as a marker for follow up, the literature lacks clear data about its interpretation as a clinical marker.We don't have clearly set prognostic rules and cutoff points especially about the rate of bilirubin decrease following biliary drainage procedures.We conducted a retrospective study to determine the likely factors that affect bilirubin levels following the interventional relief of obstructive jaundice.

Material-Method: We retrospectively analyzed data from 73 patients with obstructive jaundice who underwent interventional drainage procedures over a time period of 4 years in a tertiary healthcare center.

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Results: Decrease in the bilirubin levels was most rapid in the first 48 hour following the drainage. From the analyzed variables, only age and selected type of the drainage procedure significantly affected the rate of bilirubin decrease in our patient group. We failed to establish cutoff points that can accurately predict the patients with slower bilirubin decrease.

Conclusion: Serum bilirubin level is an important and commonly used marker predicting the success of treatment and the prognosis of the patients with obstructive jaundice. Type of drainage and the age proven to significantly affect the rate of bilirubin decrease regardless of underlying pathology.

Keywords: Bilirubin, drainage, obstructive jaundice

Introduction

Obstructive jaundice (OJ) is a serious condition which should be treated with interventional drainage procedures. Cholelithiasis being the major cause, there is a myriad of benign and malignant diseases and conditions causing OJ [1].

Measuring serum bilirubin levels is crucial in the setting of OJ and often used as a marker for follow up after interventional relief of jaundice. However, despite its major role as a marker for the follow up of these patients, the literature lacks data about factors affecting serum bilirubin levels after drainage procedures [2,3]

In this retrospective study; we aimed to evaluate factors that may be affecting the rate or pattern of bilirubin reduction following drainage procedures and establish a baseline data for the planning of our future prospective study on the subject.

Material Method

A database search using ICD-10 codes was conducted, covering a time period between June 2013 and December 2017, in the patient database of a tertiary healthcare center. Of the initially retrieved 109 patient records, 36 were excluded. Exclusion criteria were, faulty diagnostic code entries, patients' not receiving interventional drainage procedures and/or refusal of treatment.

Medical recordings of remaining 73 patients were evaluated and demographics, disease related data as well as treatment methods and results were recorded for each patient.

Total bilirubin (TB), aspartate aminotransferase (AST), alanine aminotransferase (ALT) measurements throughout their hospitalization period were recorded. These biochemical markers were measured quite regularly in the first 5 days following the procedure, however measurements became irregular after 6 days. Thus, most of the statistical analyses focused on the postoperative 5 days. Alkaline phosphatase and gamma-glutamyl transferase levels were omitted as they were not measured systematically in our patient group.

Patients were divided into subgroups according to the etiology of OJ and type of the drainage procedure. Interventional procedures were classified according to two major properties of drainage: direction of drainage (external or internal) and invasiveness of the procedure (minimally invasive or surgery). External drainage procedures consisted of surgical t tube drainage or catheter drainage via percutaneous transhepatic cholangiography (PTC). Internal drainage procedures consisted of surgical bilio-enteric anastomoses and stenting or stone extraction with endoscopic retrograde cholangiopancreatography (ERCP).

None of the patients received medical therapy of any kind that affects bilirubin levels. Figure 1 shows patient classification algorithm and the number of patients in each sub group.

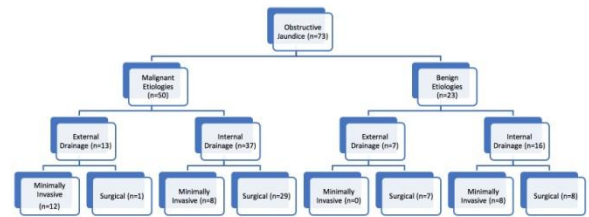


Figure 1: Classification of the patients

The approval was obtained from the ethical committee of our hospital dated 11.02.2017 and decision number 14. Patient-informed consents for publication were obtained from all patients.

Statistical Analysis:

Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) version 25 by International Business Machines Corporation (IBM) in Armonk, New York, United States. A p-value of less than 0.05 was considered statistically significant.

Results

Average age of the patient group was 67 ranging from 36 to 91. Sex distribution was fairly homogenous: 50.7% male, 49.3% female. Etiologies causing OJ varied widely among patients; from iatrogenic bile duct injuries to the tumors of the bile duct tree. Majority of the patients had OJ owing to malignant etiologies (68.5% n=50). Accordingly, half of the drainage procedures (50.7% n=37) were surgical internal drainage procedures (bilio-enteric anastomoses). Table 1 summarizes demographics, etiologies and procedure types.

Table 1: Summary of the cases

Patient Characteristics		# of Cases	Percent age
Sex	Male	37	50.7
	Female	36	49.3
Drainage Procedure	External, Minimally Invasive	12	16.4
	External, Surgical	8	11
	Internal, Minimally Invasive	16	21.9
	Internal, Surgical	37	50.7
	Periampullary or Pancreatic Tumors	37	50.7
Etiology	Tumors of the biliary tree	13	17.8
	Cholelithiasis	19	26
	Iatrogenic obstruction	4	5.5

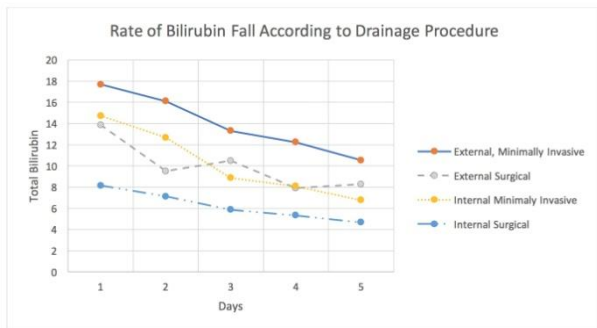
Average measured serum TB at the time of admission was 10.7 mg/dl ranging from 2.5 to 34. Average AST and ALT was 119.6 IU/L and 116.5 IU/L respectively.

The most rapid decrease in the average TB of the patient group was observed in the first 48 hours (31.7% decrease). This rate gradually dropped afterwards and 30% drop in the 2nd day was taken as an endpoint for receiver operating characteristic curve (ROC) analysis. We tested initial TB, AST, ALT measurements and the age of the patients for this end point to establish a cutoff value that predicts delay in TB decrease rate, however no significant correlation was found.

Univariate and multivariate analyses were employed to test the relation between the rate of TB decrease over time and the variables such as age, etiology of jaundice, initial TB, AST and ALT levels and type of the drainage procedure. Among these tested variables, only age and type of the drainage procedure significantly affected the rate of TB decrease (p values 0.007 and 0.021 respectively).

Rate of TB fall was significantly slower in the older patients and external drainage procedures were significantly faster by means of lowering TB levels. Figure 2 shows the decreasing rate of TB over time according to the type of drainage procedures.

Figure 2: Rate of bilirubin fall according to the type of drainage procedure



Discussion

Obstructive jaundice is a serious condition with possible devastating consequences such as coagulopathy, progressive hepatocellular dysfunction and cholangitis [3,4]. Therefore, prompt treatment with interventional measures and rapid resolving of the jaundice is crucial for these patients.

Serum TB level emerges as a practical marker that can be employed for follow up after relief of OJ. It is readily available virtually in almost every healthcare center and commonly used by physicians for evaluating the success of the drainage procedures.

Early intervention in the event of drainage failure or predicting the course of a successful treatment is important as it may affect the prognosis of the patient and delay possible subsequent treatments such as chemotherapy for the patients with malignant cholestasis [3,5].

However, despite its common utilization and importance as a marker; the literature heavily lacks data about the course of serum bilirubin levels following the relief of OJ and clinical predictions often relies on anecdotal knowledge and educated guessing. In addition, there is also no data supporting its utilization as a prognostic marker predicting the success of a drainage procedure. Predicting the success of drainage especially becomes important after internal drainage procedures, where monitoring options are limited. Hydroxy-iminodiacetic acid (HIDA) scan is offered as an alternative for monitoring the success of internal drainage procedures [2]. However, it is not that readily available especially in developing countries like Turkey.

Shortly put; there is simply no agreed pattern or cutoff points about the decrease rate of TB that can reliably predict the success of a treatment or prognosis in the setting of OJ.

A valuable study by Weston et al. on 156 patients with malignant OJ, suggests a 6-week cutoff point for patients with an initial TB level 10 mg/dl and higher and 3 weeks for patients with less than 10 before trying a second intervention with ERCP [3]. However, this study focuses on only internal drainage by stenting with ERCP. Another study by Irabor et al., evaluates preliminary results of only 7 patients following drainage with surgical procedures [2]. This manuscript reports an expected TB decrease of 30% on the post interventional 2nd day. Similar pattern of decrease was also observed (31.7% on the 2nd day) in our larger and heterogeneous group of patients. Another study by Cildag et al. also reports a rate of decrease (38.4%) on the 2nd day, supporting these results.

We studied other possible variables that may affect the TB levels following drainage procedures. Previous studies found that some variables such as, diffuse liver metastases, elevated INR and initial bilirubin levels significantly affect the rate of TB decrease after drainage [2,3,5].

In our group of patients, the only variables that affected the rate of TB decrease were the age of the patient and selected type of drainage. Age emerges as a different variable when compared to other variables tested in aforementioned studies (p=0.007).

It may be affecting the rate owing to the decreased functional capacity of the liver in the elderly. However, we couldn't find any correlation with AST and ALT levels, which also roughly indicate the general condition of the liver.

As mentioned earlier, selected type of drainage also significantly affected the rate of TB decrease ($p=0.021$). This variable was not studied before as the manuscripts focused on the results of only one type of drainage procedure [2,3,5]. External drainage procedures caused a more rapid decrease in TB levels in our patient group. This may be due to the physiologic effect of draining the bile directly out of the body preventing it from entering enterohepatic cycle as well as bypassing the bilio-enteric junction (sphincter of Oddi or anastomosis) which may be narrowed due to possible edema following interventional procedures. On the other hand, despite us not finding any correlation with the initial TB levels and the rate; patients requiring external drainage procedures were usually the patients with higher initial TB levels. This proportional difference may also have contributed to seemingly rapid decrease in this group of patients as other studies suggested [2,3,5].

Conclusion

Serum bilirubin level is an important and commonly used marker predicting the success of treatment and the prognosis of the patients with OJ. The literature, including text books, lacks information on the interpretation of serum bilirubin levels after relief of obstructive jaundice. From another perspective, there is also lack of evidence supporting the use of serum bilirubin level as a marker for predicting the success of treatment and the prognosis.

On the other hand; selected type of drainage and the age of the patients proven to significantly affect the rate of bilirubin decrease regardless of underlying pathology.

The drawbacks of this study are its retrospective fashion and irregularity in measurements of bilirubin levels in a relatively small group of patients. Well planned prospective studies with larger group of patients are needed to elucidate the role of serum bilirubin level in the follow up period of the patients. With the help of the data from previous studies and our study; we are planning a prospective study hoping to find more clear results and certain cutoff points that may help physicians to easily make more accurate clinical predictions.

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