Article published online: 2024-01-31

Review Article

How Dexamethasone Affects Necessity for Surgical Intervention for Chronic Subdural Hematoma: Systematic Review and Meta-Analysis

Amit Agrawal[1] Amit Gupta[2] Rakesh Mishra[3] Oday Atallah[4] Md Moshiur Rahman[5] Saikat Das[6] Luis Rafael Moscote-Salazar[7] Prasad Krishnan[8] Ved Prakash Maurya[9]

[1] Department of Neurosurgery, All India Institute of Medical Sciences, Saket Nagar, Bhopal, Madhya Pradesh, India
[2] Department of Neurosurgery, GSVM Medical College, Kanpur, Uttar Pradesh, India
[3] Department of Neurosurgery, Bhopal Memorial Hospital and Research Centre, Bhopal, Madhya Pradesh, India
[4] Department of Neurosurgery, Hannover Medical School, Hannover, Germany
[5] Department of Neurosurgery, Holy Family Red Crescent Medical College, Dhaka, Bangladesh
[6] Department of Radiation Oncology, All India Institute of Medical Sciences, Saket Nagar, Bhopal, Madhya Pradesh, India
[7] Neurocritical Care, Colombian Clinical Research Group in Neurocritical Care, Bogota, Colombia
[8] Department of Neurosurgery, National Neurosciences Centre, Calcutta, West Bengal, India
[9] Department of Neurosurgery, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

Address for correspondence Amit Agrawal, MCh, Department of Neurosurgery, All India Institute of Medical Sciences, Saket Nagar, Bhopal 462020, Madhya Pradesh, India (e-mail: dramitagrawal@gmail.com; dramitagrawal@hotmail.com).

Indian J Neurotrauma

Abstract

The effectiveness of dexamethasone in managing chronic subdural hematoma (cSDH) patients remains uncertain although the drug is widely used in this condition. The present systematic review aims to understand the role of dexamethasone in reducing the need for surgery in cSDH patients. This study was conducted as per the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched the electronic databases of PubMed, SCOPUS, Cochrane Central Register of Controlled Trials (the Cochrane Library), and ScienceDirect with a predefined search strategy. The population consisted of cSDH patients older than 18 years and treated primarily with dexamethasone. The primary outcome was the need for surgery after dexamethasone therapy in cSDH patients. The meta-analysis of a group of patients was done with the invariance method to estimate the pooled odds of the requirement for surgery after dexamethasone therapy. In the studies with a one-to-one comparison of dexamethasone with placebo/observation, the Mantel–Haenszel statistics were used to determine the odds of surgery. The quality of the studies was assessed with the Newcastle–Ottawa scale (NOS) and the Cochrane risk of bias tool was used to assess the risk of bias in randomized studies. In total, 598 studies were obtained from the database search and after applying the inclusion and exclusion criteria, 10 studies were finally selected for the qualitative and quantitative synthesis. One of the 10 studies was a randomized controlled trial (RCT), while the rest were observational studies. There were 653 patients who received the primary dexamethasone therapy. Of these, 388 patients did not require surgery, while 256 needed surgeries after the therapy. The pooled estimate of requirement for surgery after dexamethasone therapy was 0.41, with a 95% confidence interval of 0.37 to 0.45. A meta-analysis of the one-to-one comparison from three

Keywords
- dexamethasone
- nonsurgical
- subdural hematoma
- chronic
- meta-analysis

DOI https://doi.org/10.1055/s-0044-1779288.
ISSN 0973-0508.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

included studies showed a higher need of surgery in the (comparator) placebo/observation group than in the dexamethasone group with odds ratio of 7.16 (95% confidence interval: 2.21–23.13, with $p = 0.0001$). In addition, we identified the gaps in literature, and the complications and mortality reported in the studies. Dexamethasone is effective in reducing the requirement for surgery in some selected cSDH cases, although many patients still require surgical intervention.

Introduction

Chronic subdural hematoma (cSDH) is a commonly managed clinical entity in neurosurgical practice. Due to increased life expectancy and demographic effect of aging, it is anticipated that there will be a further increase in cases of cSDH.[1–3] The management options for cSDH include surgical intervention (trepanation or burr hole craniostomy) in symptomatic cases and conservative management in asymptomatic patients. cSDH is diagnosed in individuals older than 70 years and individuals with coagulation disorders and alcohol abuse.[4] Despite this increase in the incidence of cSDH, there is no consensus on the treatment options, and they vary on a regional, national, and international level.[2] Asymptomatic cSDH is often treated conservatively. In contrast, symptomatic cSDH is recognized worldwide by neurosurgeons as a surgical emergency requiring prompt treatment to prevent brain herniation. Despite the large number of studies, the decision to administer different treatment modalities depends on the treating physician's expert opinion, and no consensus exists. There are a lot of variations in the medical and surgical practice and the duration of surgery in cases of failed medical management. Therefore, research question about the role of dexamethasone as a stand-alone treatment option in cSDH and identification of the variables that might be associated with the failed medical therapy is relevant. This was the primary objective of the present study. The secondary objective was to determine the types of evidence available and gaps in the literature related to the question.

Table 1 Details of search strategy

Database	Search terms
PubMed	((“dexamethason”[All Fields] OR “dexamethasone”[MeSH Terms] OR “dexamethasone”[All Fields] OR “dexamethasone s”[All Fields] OR “dexamethasones”[All Fields]) AND (“subdural haematoma”[All Fields] OR “hematoma, subdural”[MeSH Terms] OR (“hematoma”[All Fields] AND “subdural”[All Fields]) OR “subdural hematoma”[All Fields] OR (“subdural”[All Fields] AND “hematoma”[All Fields]))) AND (1000/1/1:2023/6/14[pdat])
Scopus	TITLE-ABS-KEY (dexamethasone AND subdural AND hematoma)
Cochrane	Title, abstract, keywords: dexamethasone subdural hematoma
ScienceDirect	Title, abstract, keywords: dexamethasone subdural hematoma

Objectives

The present systematic review aims to study the need for surgery in dexamethasone as a stand-alone treatment in cSDH and to identify factors associated with the failed medical management requiring additional surgery. The secondary objective was to map the key concepts and types of evidence available in gaps in the literature related to the question.

Methods

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[5] and the Cochrane Manual of Systematic Reviews and Meta-analyses.[6]

Eligibility Criteria

Inclusion Criteria

- Studies with at least one arm with the dexamethasone alone group.
- Age 18 years or older.
- *Study design:* randomized controlled trials (RCTs), quasi-randomized controlled studies, and prospective and retrospective observational studies.

Exclusion Criteria

- Studies that did not include at least one dexamethasone group.
- *Study design:* case series, case reports, letters, editorials, comments, animal studies, and studies published in languages other than English.

Outcome Measure

Patients on dexamethasone alone requiring surgical intervention.

Search Strategy

We searched the PubMed, SCOPUS, Cochrane Central Register of Controlled Trials (the Cochrane Library), and ScienceDirect databases with predefined search terms (►**Table 1**). The reference lists of the included studies were evaluated for potentially eligible studies. We included studies including RCTs, quasi-randomized controlled studies, and prospective and retrospective observational studies. Case series, case reports, letters, editorials, comments, animal studies, and studies published in languages other than English were excluded. No restrictions were placed on the time, setting, and source of publication.

Data Synthesis

Two investigators (A.A. and O.A.) independently evaluated the studies and extracted data in a predesigned proforma as per the inclusion criteria. The details included were study ID, authors, year, country, inclusion criteria, sample size in each group, age, gender, dose of dexamethasone, treatment groups, reported outcomes, need for surgery in patients who received dexamethasone group, any complications, details of the Markwalder Grading Scale (MGS)[7] at admission, the Glasgow Outcome Scale, or any other scale used to categorize cSDH. The Cochrane Collaboration's tool[8] was used for assessing the risk of bias in randomized studies. The Newcastle–Ottawa Quality Assessment Scale[9] was used to assess the quality of the research included; studies with a score of 9 were regarded to have good methodological quality (7–9 points). For observational studies, ratings in the range of 6 were considered of moderate quality, whereas scores of 5 or less were considered of low quality. The authors were contacted for missing data. Consultation by consensus helped clear up any confusion.

Statistical Analysis

The statistical analysis for meta-analysis of the included studies was performed for one group in R and for one comparison between dexamethasone and placebo/observation group in RevMan. For meta-analysis of one group, the inverse variance method was used with Logit transformation, DerSimonian–Laird estimator for tau-squared and Clopper–Pearson confidence interval. The overall effect was calculated as odds ratio (OR) with its 95% confidence interval (95% CI). Random effects model was used, and heterogeneity was assessed by Cochrane Q test and I^2 test, with a threshold of p-value less than 0.10 or I^2 more than 50% indicating substantial heterogeneity. Publication bias was displayed by a funnel plot if the number of included studies were more than 10.

Results

The datasets search resulted in a total of 598 results. After removing duplicates, 468 records were screened and 432 studies were excluded (►**Fig. 1**). Full text was screened for 36 studies, of which 26 studies were excluded with reasons[10–35] and 10 studies were included[1,36–44] in the systematic review and meta-analysis (►**Tables 1**–**3**). The characteristics of the included studies are shown in ►**Table 3**.

Characteristics of Individual Studies

Sun et al

Study Site and Design

The study by Sun et al[43] was a single-center prospective cohort study conducted between 1998 and 1999.

Population

The patients were older than 18 years with symptomatic cSDH.

Intervention

A dose of 4 mg dexamethasone four times a day for 3 weeks was prescribed. Surgical management included burr hole and evacuation within 2 days of starting dexamethasone therapy and dexamethasone was continued for 2 weeks

Outcome

Glasgow Outcome Scale (GOS) at 6 months. Failure of treatment was defined as neurological deterioration with radiological evidence of re-accumulation of cSDH.

Results

A total of 112 patients were included in the study, of which 26 patients were treated with dexamethasone alone, 69 with surgery and 2 weeks of dexamethasone, 13 with surgical drainage alone, and 4 patients received only observation. One out of 26 patients with dexamethasone therapy required surgery after 1 month. Two patients in the observation group required surgery. In all, 84% of patients treated with dexamethasone only had good GOS at 6 months, while 91% patients who had a surgery and with dexamethasone had good GOS at 6 months. In the surgery alone group, 77% had good outcome and 50% had good outcome in the observation alone group at 6 months of follow-up. The main complication observed was hyperglycemia.

Delgado-López et al

Study Site and Design

This was a single-center study comprising 122 cSDH patients reviewed retrospectively.[36]

Population

In the study, patients with MGS scores of 1 to 2, that is, alert, oriented, tired, or disoriented with possible variable neurological deficits were given dexamethasone, while patients with MGS scores of 3 to 5 who are stuporous or comatose were assigned to the surgery group.

Intervention

The authors used dexamethasone 4 mg three times a day and reassessed the patients after 48 to 72 hours; patients who did not show any improvement were then reassigned to the surgery group. Other responders were ambulated and discharged with a tapering dose of steroids. Follow-ups were done after 6 weeks and at complete cure or clinical and radiological stabilization. The surgical protocol consisted of twist drill mini-craniostomy and subdural drainage. In the case of nonimprovement of patients, dexamethasone was used after the drainage.

Outcome

MGS at discharge. Length of hospital stay.

Results

The median age of the patients was 78 years (range: 25–97 years). Forty-seven patients were older than 80 years, while 98 patients were older than 70 years. In all, 101 patients were given dexamethasone, 19 had surgery, and 2 were untreated. Of the patients who were given dexamethasone, 76 were given

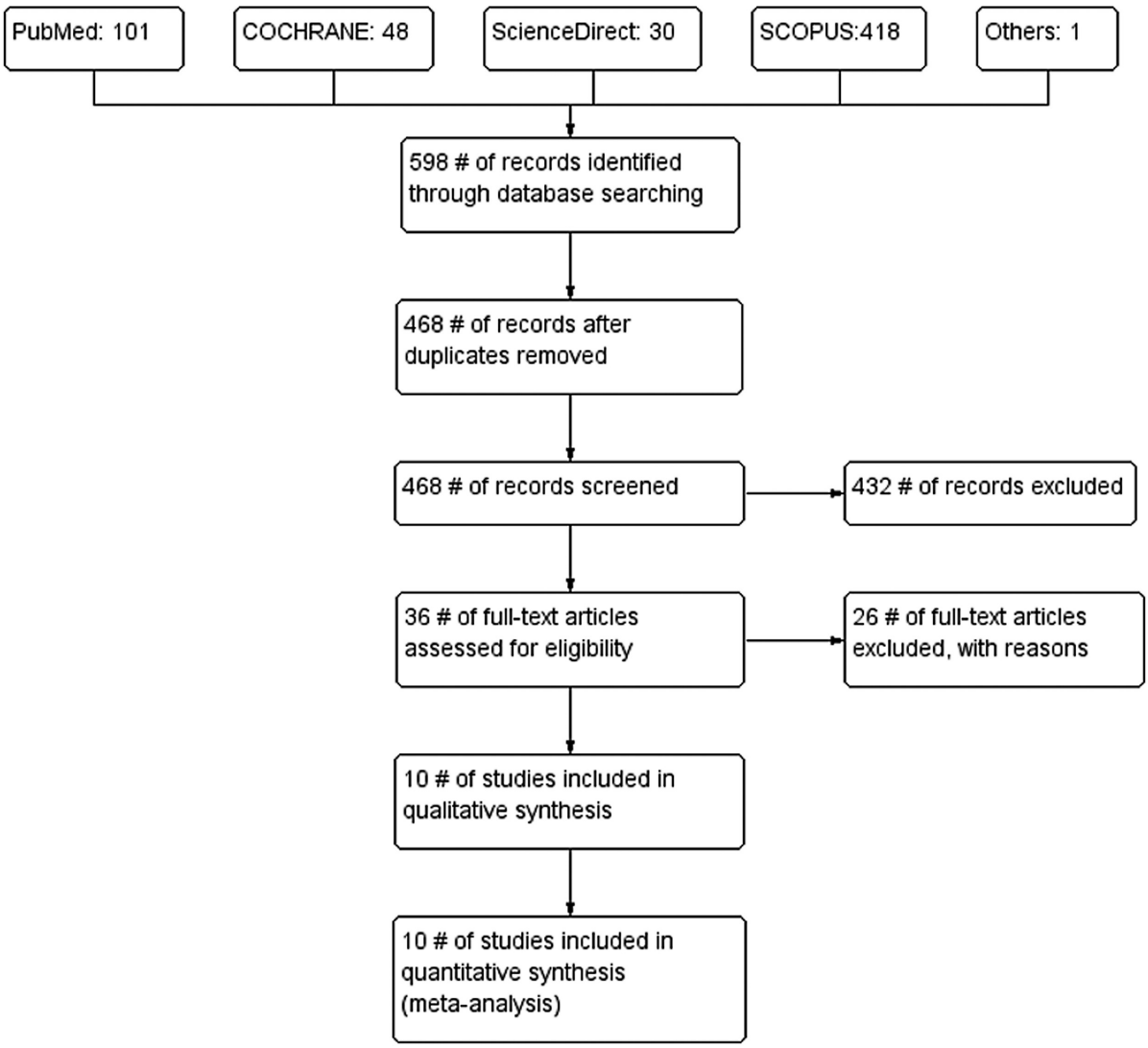

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

dexamethasone alone, while 25 had dexamethasone in combination with surgery. Twenty-two patients initially assigned dexamethasone required surgery, and 3 more needed a second drain and posterior craniotomy. Ninety-seven of 101 patients with dexamethasone treatment achieved favorable outcomes as defined by MGS scores of 0, 1, or 2. Seventy-four of 76 patients who were given dexamethasone alone had good results. Thirty-four patients developed complications, mainly comprising hyperglycemia and nosocomial infection. However, the complications were not reported individually for the groups. The median length of hospital stay was almost similar in the dexamethasone and surgery groups.

Thotakura and Marabathina

Study Site and Design

This is a prospective single-center study conducted from April 2013 to May 2015.[44]

Population

cSDH patients with Glasgow coma scale (GCS) score 15/15.

Intervention

Dexamethasone 4 mg three times a day for 3 days was prescribed. Neurological evaluation was done at 72 hours and the patients who did not show improvement were subjected to surgery. Patients who showed improvement were discharged on tapering dose of steroids for 4 weeks as tab prednisolone 10 mg three times a day for 1 week, tab prednisolone 10 mg twice a day for 1 week, tab prednisolone 5 mg twice a day for 1 week, tab prednisolone 5 mg once a day for 1 week, and then stopped. Surgery consisted of single parietal burr hole and evacuation of the cSDH with subdural drain placement.

Outcome

Radiological and neurological cure assessed at 6 weeks was defined as success of the steroid treatment.

Table 2 Excluded studies with reasons

Study	Reason for exclusion
Rudiger et al[26]	Case report
Chan et al[11]	No dexamethasone alone group
Qian et al[25]	Dexamethasone was used after surgery
Zhang et al[35]	Recurrent hematoma
Davis-Wilkie[13]	Protocol
Edlmann et al[16]	Protocol
Huang et al[20]	Case series
Jong[22]	Protocol
Kolias[23]	Protocol
Fan, 2020[17]	In vitro study
Hutchinson, 2020[21]	No dexamethasone alone group
Mebberson, 2020[24]	No dexamethasone alone group
Wang, 2020[33]	No dexamethasone groups
Diener, 2021[14]	Non-English
Fan et al[18]	In vitro study
Holl et al[19]	Conference abstract
Simon[28]	Non-English
Tariq and Bhatti[30]	Dexamethasone was used after surgery
Vetter[31]	Non-English
Wang et al[32]	Animal model
Yuan et al[34]	Case series
Edlmann et al[15]	Subgroup from Dex-CSDH trial[21]
Saul et al[27]	Practice article
AbdelFatah[10]	Case series
David et al[12]	Comment
Sioutas et al[29]	Dexamethasone and statin given together

Results
In all, 26 patients were included in the study with similar underlying demographic, neurological, and radiological characteristics. Ten of 26 patients required surgery after 72 hours. Five more were subjected to surgery at 3 to 6 weeks of follow-up due to recurrence of symptoms and nonresolution of cSDH radiologically. Finally, 11 of 26 patients got complete resolution of the symptoms and radiological cure at 6 weeks of follow-up. Two patients developed complications of hyperglycemia and gastritis related to steroids.

Prud'homme et al

Study Site and Design
This was a single-center placebo controlled double blind RCT conducted between January 2007 and May 2009.[42]

Population
cSDH patients aged more than 18 years with MGS scores of 0 to 2.

Intervention
A dose of 12 mg dexamethasone per day for 3 weeks and then tapered over next 1 week. Total dose of dexamethasone administered was 267 mg.

Control
Placebo.

Outcome
Succes of medical management in avoiding surgery during 6 months following enrolment or interruption of medical management due to serious adverse effect.

Results
The study included 20 participants, 10 in the dexamethasone group and 10 in the placebo group. One patient in the dexamethasone group needed surgery between 3 and 18 days after enrolment, while 3 patients had serious adverse effects. In the placebo group, three patients needed surgery. Six of 10 patients in the dexamethasone group had treatment success at 6 months, while 7 in the placebo group had treatment success.

Fountas et al

Study Site and Design
This retrospective single-center study was conducted between January 2012 and December 2016.[37]

Population
In total, 171 adult symptomatic cSDH patients with a follow-up period greater than 3 months were included.

Intervention
Patients were divided into three groups: dexamethasone alone, dexamethasone as adjunct to burr hole, and burr hole alone. Dexamethasone was given 8 mg thrice daily for 1 week and then tapered over the next week.

Outcome
Recurrence occurred in 1, 10, and 3 patients in the dexamethasone as an adjunct to burr hole, burr hole alone, and dexamethasone alone groups, respectively. Mortality was one, eight and zero in the dexamethasone as an adjunct to burr hole, burr hole alone, and dexamethasone alone groups, respectively.

Results
One hundred seventy-one patients were included in the study, with a mean age of 76.4 ± 9.3 years. Ten patients were treated with dexamethasone alone, 136 with burr hole alone, and 25 with dexamethasone as an adjunct to the burr hole treatment. The mean length of hospital stay was 7.7 ± 3.2, 7.1 ± 4.9, and 3.5 ± 2.0 days for the

Table 3 Characteristics of included studies

Study	Country	Study type	Inclusion criteria	Exclusion criteria	Markwalder chronic subdural hematoma grading scale (MGS)	Gender	Age (y)	Dexa doses	Treatment groups Dexamethasone alone	Primary outcome	Need for Surgery	Complications	Mortality
Sun et al[43]	Hong Kong	Prospective	≥ 18 y	Asymptomatic with a clot thickness of < 5 mm		57.1% males	Median 75	4 mg 4 times a day for 21 d	26	No significant difference in retreatment rates between with or without dexamethasone	1	Mortality rate: 4% ($n=1$) Complications: 0%, no patients were reported to develop significant acute complications	1
Delgado-López et al[36]	Burgos	Comparative, retrospective	MGS 1–2 to the dexamethasone protocol, MGS 3–4 to the surgical protocol	No	MGS left untreated	69% males	Median 78	4 mg every 8 h, reevaluation after 2–3 d, slow tapering	101	Favorable outcome in 96% in dexamethasone group, 93.4% in surgery group	22	Mortality rate: 0.8% Complications rate: 27.8%; mainly hyperglycemia	0
Thotakura and Marabathina[44]	India	Prospective	cSDH with GCS 15/15	Acute SDH		76.9% males	Mean 60	4 mg three times a day for 3 d, tapering tab prednisolone over 4 wk	11	10 patients did not show any improvement in 72 h of steroid therapy and needed surgery. Five more needed surgery at 3–6 wk. One of the operated patients developed recurrence that was treated with steroids	15	Hyperglycemia ($n=1$); gastritis ($n=1$)	0
Prud'homme et al[42]	Canada	Randomized controlled trial	≥ 18 y	Contraindication for steroids, already started steroid treatment for other indication, previous neurosurgical surgery, concomitant cerebral pathology		90% males	Mean 70.8	12 mg (4 mg three times a day) for 3 wk followed by tapering: 8 mg for 48 h, 4 mg for 48 h, 2 mg for 48 h, 1 mg for 24 h	10 (3 patients had significant complications) Effectively 7 patients	Lower rate for surgical intervention in the dexamethasone group. High rate of side effects in dexamethasone group	1	Mortality rate: 20% ($n=2$) Complications: 90% ($n=9$) Hyperglycemia 44.4% ($n=4$), hypertension 11.1% ($n=1$), pulmonary embolism 11.1% ($n=1$), cellulitis 11.1% ($n=1$), pulmonary edema 11.1% ($n=1$), suicide 11.1% ($n=1$)	2
Fountas et al[37]	Greece	Technical notes, retrospective	Patients with follow-up at least 3 mo	Follow-up < 3 mo		70% males	Mean age 76.4	8 mg 3 times a day for 1 wk, then gradually reduced every 2–3 d and discontinued over 5–7 d	10	Recurrence in dexamethasone group most significant, patients with surgery and dexamethasone the best outcome, midline shift/preoperative hematoma volume/postoperative GCS associated with recurrence	3	Mortality rate 0% No information about complications	0
Papacocea[41]	Romania	Retrospective	≥ 18 y, hypo- or iso-dense component, mRS 1–3	< 18, mRS > 3, hyperdense component on CT scan		31.5% males	Mean 71	4 mg twice daily on days 1–7, 4 mg once a day on days 8–14, 4 mg once every 2 d on days 15–21	22	Low need to surgery and low complications rate in the dexamethasone group	9	Mortality rate: 4.5% ($n=1$) Complications: 36.3% ($n=8$) Urinary tract infection 13.6% ($n=3$), worsening of motor deficit 12.5% ($n=2$), infection with *C. difficile* 4.5% ($n=1$), bronchopneumonia 4.5% ($n=1$)	1

Table 3 (*Continued*)

Study	Country	Study type	Inclusion criteria	Exclusion criteria	Markwalder chronic subdural hematoma grading scale (MGS)	Gender	Age (y)	Dexa doses	Treatment groups Dexamethasone alone	Primary outcome	Need for Surgery	Complications	Mortality
Miah et al[40]	The Netherlands	Retrospective	≥ 18 y	MGS 0 were excluded		78% males	Mean 72.5	6–8 mg/d with a median duration of 12 d	60	Favorable mRS and MGS in the surgery group, more complications and long hospital stay in the dexamethasone group	50	Mortality rate: 10% (n =6) Complications: 55% (n =33) Delirium (n = 12), hyperglycemia (n = 11), urinary tract infection (n = 7), epileptic seizure (n = 5), and other	6
Holl et al[38]	The Netherlands	Retrospective		When subdural hyperdense components were seen on CT comprising >1/3rd of the hematoma	MGS 1–3	70.3% males	Mean 75	8 mg twice a day for 1 wk, then tapered by half every 3 d until a dosage of 0,5 mg once daily on days 20–22 and ended on day 23	283	Additional surgery less frequently in patients using antithrombotic and patients with trabecular hematoma	107	Mortality rate 12% (n = 34) Complications: 42.4% (n = 62) Hyperglycemia 17.1% (n = 25), infection 15.8% (n = 23), thrombotic events 4.8% (n = 7), seizure 4.2% (n = 4), pulmonary embolism 1.8% (n = 3)	34
Ahmed et al[1]	Egypt	Retrospective	Newly diagnosed cSDH MGS 1–2	Recurrent cSDH, MGS 3–4, acute SDH, MGS 0	MGS 1–2	63.3% males	Mean 62.60	8 mg twice a day for 4 d then tapered by half every 3 d and stopped on 20th d	30	GCS at two weeks, one month, three and six months; Requirement of additional surgery	9	N = 8 had nonserious complications; mild hyperglycemia (n = 4); mild gastritis (n = 2) oral candidiasis (n = 1); severe hyperglycemia (n = 1)	1
Miah et al[39]	The Netherlands	Randomized controlled trial				75% males	Mean 76	DX 16 mg twice daily on days 1–4, 8 mg on days 5–7, 4 mg on days 8–10, 2 mg on days 11–13, 1 mg on days 14–16, 0.5 mg on days 17–19, stopped at day 20	85	Which hematoma subtype is favorable for dexamethasone therapy? Need for additional surgery	48	Mortality rate: 7% Complications:57% (n = 46), hyperglycemia 16% (n = 13), delirium 16% (n = 16), infection 12% (n = 10), electrolyte disturbance 7% (n = 6), insomnia 5% (n = 4), behavioral disturbance 5% (n = 4), vomitus 4% (n = 3)	6

Abbreviations: cSDH, chronic subdural hematoma; DX, dexamethasone; GCS, Glasgow coma scale; mRS, modified Rankin scale; MGS, Markwalder grading scale; SDH, subdural hematoma.

dexamethasone as an adjunct to burr hole, burr hole alone, and dexamethasone alone groups, respectively.

Papacocea et al

Study Site and Design
This single-center retrospective study conducted between January 2016 and December 2017.[41]

Population
cSDH patients aged more than 18 years with modified Rankin scale (mRS) score of 1 to 3 were divided into two groups: those who received dexamethasone and those who did not receive dexamethasone.

Intervention
A dose of 8 mg dexamethasone per day for 1 week followed by 4 mg per day for the second week followed by 4 mg once every 2 days in the third week.

Outcome
Need for surgical intervention at 3 weeks after the dexamethasone therapy.

Results
Thirty-eight participants in the study were divided into two groups: 22 in the group who received dexamethasone and 16 in the group who did not receive dexamethasone. Nine out of 22 patients who received dexamethasone underwent surgery between days 3 and 12, while 13 of 16 who did not receive dexamethasone underwent surgery between days 3 and 8. The complications and morbidity rates were similar in the two groups.

Miah et al

Study Site and Design
This retrospective multicenter study was conducted between January 2014 and December 2016.[40]

Population
Symptomatic cSDH patients aged more than 18 years with MGS scores of 1 to 2. Asymptomatic patients with MGS score of 0 and MGS scores of 3 to 4 requiring emergency surgery were excluded.

Intervention
A dose of 3 to 4 mg dexamethasone twice daily with or without bolus was prescribed. The expert opinion was bolus administration of dexamethasone. Surgery consisted of burr hole evacuation with the placement of a subdural drain. Surgery was done in patients not responding or deteriorating with dexamethasone and by the expert opinion.

Outcome
The primary outcome was an mRS and MGS at 3 months. Secondary outcomes were mRS and MGS at discharge and follow-up, additional surgeries, and crossover of medically managed patients to surgery.

Results
Sixty patients received primary surgery without dexamethasone, and 60 patients received prior dexamethasone therapy. At 3 months, 70% in the immediate surgery group and 76% in the primary dexamethasone group had a favorable outcome (mRS score of 0–3). Twenty-two percent in the prior surgery group and 12% in the primary dexamethasone group had recurrence at 6 months. Eighty-three percent of patients (50/60) received primary dexamethasone therapy crossover to surgery after a mean duration of 6 days, and therefore, 17% of patients were able to evade the surgery, of which 8 had an improved MGS score at discharge, and 2 had unchanged scores. The rate of complications was lower in the primary surgery group (35%) versus the primary dexamethasone group (55%). The mortality was similar among both groups, and the length of hospital stay in the primary dexamethasone group was twice that in the surgery group.

Holl et al

Study Site and Design
This was a retrospective multicentric study conducted between January 2008 and December 2018.[38]

Population
The patients were adults with cSDH. The patients with hyperdense components with more than one-third of the hematoma volume were excluded.

Intervention
Dexamethasone in tapering doses in symptomatic cSDH patients is defined as MGS scores of 1 to 3. The amount of dexamethasone was 8 mg twice daily for 1 week, then tapering with the end of treatment on day 23.

Outcome
Need for additional surgery.

Results
Two hundred eighty-three patients were included in the study, of which 146 received one course of dexamethasone, 30 received more than one course of dexamethasone, and 107 received additional surgery after dexamethasone. The mean age of the participants was 70 years, with a standard deviation (SD) of 10. The need for further surgery was more in patients with MGS score of 2, using statins, more significant midline shift, larger hematoma thickness, bilateral hematoma, and separated type of hematoma. Additional surgery was less common in patients with a trabecular pattern on cSDH and using antithrombotic. The mean duration of dexamethasone therapy in the study was 30 days, and the time from the dexamethasone therapy to surgery was 12 days. The main complications were infection, hyperglycemia, pulmonary embolism, thrombotic events, and seizures. The complication

rate of infection was 24.4% in all the patients, 15.8% in the single course of dexamethasone only group, 40% in the group with additional course of dexamethasone, and 31.8% in dexamethasone with surgery group. Mortality was 17 patients in the single course of dexamethasone, 5 patients in dexamethasone and an additional course of dexamethasone group, and 12 patients in the group requiring further surgery.

Ahmed et al

Study Site and Design
This single-center retrospective study was conducted between March 2020 and February 2022.[1]

Population
Newly diagnosed adult patients with symptomatic cSDH with MGS scores of 1 to 2.

Intervention
A dose of dexamethasone 8 mg twice a day for 4 days and tapering over till the 20th day. Surgical procedure consisted of single burr hoe craniostomy at the maximum site of hematoma thickness.

Outcome
GCS at 2 weeks, 1, 3, and 6 months. Requirement for additional surgery.

Results
A total of 30 patients were included in the study. Nine patients required surgical intervention. Out of these nine patients, three required surgery at 3 days or less, 4 to 7, and greater than 7 days each. The mean length of hospital stay was 11.67 days.

Miah et al

Study Site and Design
This multicentric study was a part of the dexamethasone therapy versus surgery for chronic subdural haematoma (DECSA) trial conducted from September 2016 to February 2021.[39]

Population
Adult patients with MGS scores of 1 to 3 cSDH, baseline computed tomography (CT), scan and on dexamethasone primary treatment.

Intervention
Dexamethasone was given twice daily, amounting to the daily dosage of 16 mg on days 1 to 4, 8 mg on days 5 to 7, 4 mg on days 8 to 10, 2 mg on days 11 to 13, 1 mg on days 14 to 16, 0.5 mg on days 17 to 19, and stopped at day 20, resulting in a total amount of 110.5 mg dexamethasone. The surgical group consisted of burr hole craniostomy. Surgery was done, if necessary, based on the CT scan and neurological examination at 2 weeks of follow-ups or when the dexamethasone treatment was discontinued early due to clinical severity or comorbidities affecting the recovery.

Outcome
The primary outcome was identifying the cSDH subtype most responsive to the dexamethasone therapy. The secondary outcome was neurological outcome assessed by MGS and classified as unchanged, worsened, improved, need of additional surgery, and complications.

Results
Eighty-five participants with a mean age of 76 years were included in the study (SD: 11). The included patients had 114 cSDH, of which 56 were homogeneous, 8 laminar, 20 separated, and 30 trabecular. Fifty patients completed the 19-day duration of dexamethasone therapy, and in 35 patients, dexamethasone had to be terminated early because of the worsening clinical situation. After 2 weeks of dexamethasone treatment, hematoma thickness decreased by a mean of 3 mm, midline shift reversed by the standard of 2 mm, and hematoma volume was reduced by a mean of 14 mL. Hematoma thickness was reduced by a maximum of up to 5 mm in cSDH without hyperdense component, while reduction in the hematoma volume was maximally seen in the separated type of cSDH. Patients with hematoma without hyperdense components showed higher improvement rates than those with hyperdense components. Patients with separated hematoma had the lowest improvement rates. Complications were reported in 57% of patients, with falls, hyperglycemia, and delirium occurring the most. Additional surgery was required in 48 (57%) patients with the 16-day mean duration to surgery and was highest in the separated cSDH type.

Three studies had presented results from a one-to-one comparison of dexamethasone and placebo/observation.[41–43] One of the studies was an RCT,[41] while one study composed of participants who were a subgroup of an RCT.[39] The duration, dose of dexamethasone, and duration of surgery after enrolment are described in ►**Tables 4** and **5**.

Risk of Bias

The risk of bias in the RCT assessed by Cochrane risk of bias tool suggested low risk of bias in the domains of random sequence generation and allocation concealment (selection bias), blinding of participants and personnel (performance bias), and selective reporting (selection bias), while the risk of bias was unclear in the domain of detection, attrition, and other biases.[42] Quality assessment for the other included observation studies by Newcastle–Ottawa scale showed a median of 7/9, suggesting good quality in most of the studies. The quality assessment is as shown in ►**Table 6**.

Statistical Analysis (or Meta-Analysis)

In included studies, a total 653 patients received dexamethasone alone at the time of presentation. Of these, 388 patients did not require surgery and 265 patients required additional surgery at follow-up with a pooled proportion of 0.41 and 95% CI of 0.37 to 0.45 as shown in ►**Fig. 2**. In the meta-analysis of one-to-one comparison

Table 4 Details of various treatment options used in included studies

Study	Country	Treatment groups	Other treatments/comparator arm				
		Dexamethasone alone	Placebo	Surgery	Dexamethasone + adjuvant	Surgery + dexamethasone	Observation
Sun et al[43]	Hong Kong	26		13		69	4
Delgado-López et al[36]	Burgos	101	No	19 (15 drain, 4 craniotomy)	25	2	2
Thotakura and Marabathina[44]	India	11				15	
Prud'homme et al[42]	Canada	10 (3 patients had significant complications) Effectively 7 patients	10				
Fountas et al[37]	Greece	10	No	136	No	25	No
Papacocea[41]	Romania	22					16
Miah et al[40]	The Netherlands	60		60			
Holl et al[38]	The Netherlands	283	No	No	107	No	No
Ahmed et al[1]	Egypt	21				9	
Miah et al[39]	The Netherlands	37				48	

from three included studies (►**Fig. 3**), there was more need for surgery in the placebo/observation group than in the dexamethasone group with an OR of 7.16 and 95% CI of 2.21 to 23.13, with a *p*-value of 0.0001. We performed the sensitivity analysis to remove the RCT from these groups and found similar results (►**Fig. 3**). The heterogeneity computed was low.

Discussion

The use and results of dexamethasone in cSDH vary widely, ranging from stand-alone use to adjunctive therapy or surgical evacuation.[1,5–12] Due to the high chances of recurrence after surgery, the role of dexamethasone has been explored as either monotherapy or perioperative adjuvant therapy in cases of cSDH.[13] To justify the role of dexamethasone, the rationale is based on the property of dexamethasone to reduce inflammation and angiogenesis, thus reducing the chances of recurrence.[14] Although there are reports in which the role of dexamethasone is explored in the management of cSDH patients, the effectiveness of dexamethasone is still controversial.[15] As mentioned, there were evidence synthesis studies on dexamethasone as an adjunctive treatment to prevent recurrence following surgery. However, although individual primary research studies have found conflicting results supporting dexamethasone as a safe and efficacious treatment option, systematic reviews often have not found consistent results favoring dexamethasone. The vast heterogeneity in the studies, including the dose, duration, type of cSDH, population heterogeneity, and adjunctive treatment, is possibly the reason. Since the dose and duration of dexamethasone widely varied among the studies and population variation, we adopted the scoping review approach to address our research question.

Prior studies have suggested dexamethasone as a safe and effective alternative to surgical management in cSDH with equal or slightly superior effects on the clinical outcome.[11,25,36,43–45] In addition, studies have found that dexamethasone is adjuvant to surgical therapy, and a more extended dexamethasone therapy reduces the risk of recurrence.[11,25,37,46] The survey by Miah et al suggested that although several patients could evade the need for surgery with primary dexamethasone therapy, they required more extended hospital stays and a higher risk of complications.[40] However, further studies did not support the findings.[38] The emerging results could not be established as high-grade evidence in multiple systematic reviews due to high selection bias and significant heterogeneity in the individual primary research studies.

The use of corticosteroids in cSDH was initiated and extensively studied by Dr. Bender in 1974.[47] Over time, dexamethasone became a standard treatment for cSDH in Rotterdam. In 2011, it was included in regional guidelines as a primary option. Surgery is recommended if there is clinical deterioration or no improvement within 72 hours. However, no agreement exists on using dexamethasone nationally or internationally. The rationale for using steroids in managing cSDH relies on the effects of steroids on the clot membrane and neovascularisation.[48–51] In addition to the clinical outcome, radiological improvement has been studied using dexamethasone in cSDH. One study reported that the resolution of hematoma took a longer time with steroid treatment. However, patients remained clinically stable, and some patients on dexamethasone treatment needed a follow-up of up to 6 months for a radiological cure.[36]

Understanding the pathophysiology underlying the formation of cSDH had evolved from the hyperosmotic therapy to the present inflammatory theory with repeated bleeding in the subdural space.[49–52] Further studies have

Table 5 Dose, duration of dexamethasone therapy, and duration of surgery after enrolment

Study	Dose of dexamethasone	Duration of dexamethasone therapy	Criteria for decision of surgery in dexamethasone group	Subgroups assessed	No. of patients assigned dexamethasone as initial treatment	No. of patients requiring surgical intervention	Duration after dexamethasone to surgery
Sun et al[43]	4 mg/d for 3 wk	21 d	Neurological deterioration with radiological evidence of re-accumulation of cSDH	Dexamethasone only; surgery with dexamethasone; surgery only; observation	26	1	30 d
Delgado-López et al[36]	4 mg three times a day	Not mentioned	Patients not showing improvement after 48–72 h	1. Dexamethasone, dexamethasone + drain, drain + drain, drain + craniotomy 2. Markwalder grading scale and treatment options 3. Midline shift and treatment options	101	Total 25 needed surgery; 22 needed subdural drain, and 3 needed second drain and posterior craniotomy	48–72 h
Thotakura and Marabathina[44]	4 mg three times a day for 3 d followed by tab prednisolone 10 mg three times a day for 1 wk; twice a day for 1 wk, 5 mg twice a day for 1 wk; 5 mg once a day for 1 wk	3 d in nonresponders, 4 wk d in responders	Neurological examination at 72 h	1. Dexamethasone alone group 2. Dexamethasone as adjunct to surgery group	26	15	72 h in 10 patients and 3–6 wk in 5 patients
Prud'homme et al[42]	12 mg/d for 3 wk and tapered over 1 wk	28 d	Clinical status	Dexamethasone group vs. placebo	10	1	3–18 d
Fountas et al[37]	8 mg three times a day for 1 week and then tapering over 1 week	14 d	Not reported	Dexamethasone alone; dexamethasone as adjunct to burr hole; burr hole alone	10	Not reported (the authors have mentioned three recurrences in the dexamethasone monotherapy group but did not report on the treatment of the recurrent cases)	3 mo
Papacocea[41]	8 mg/d for 1 wk followed by 4 mg/d for 1 wk followed by 4 mg every alternate day for 1 wk	21 d	Clinical examination at 3 wk	Patients in dexamethasone and not on dexamethasone	22	9	21 d

(*Continued*)

Table 5 (*Continued*)

Study	Dose of dexamethasone	Duration of dexamethasone therapy	Criteria for decision of surgery in dexamethasone group	Subgroups assessed	No. of patients assigned dexamethasone as initial treatment	No. of patients requiring surgical intervention	Duration after dexamethasone to surgery
Miah et al[40]	3–4 mg dexamethasone twice daily with or without bolus. The bolus administration of dexamethasone was decided by the experts	12 d	Surgery was done in patients not responding or deteriorating with dexamethasone and also by the expert opinion	Dexamethasone primary treatment	60	50	6 d
Holl et al[38]	8 mg twice a day for 1 wk and then tapering till it was stopped on the 23rd d	22 d	Not reported	Single course of dexamethasone alone; dexamethasone with additional course of dexamethasone; dexamethasone with surgery	283	107	12 d
Ahmed et al[1]	8 g twice a day and then tapered and stopped on 20th d	20 d	Clinical examination	Dexamethasone and dexamethasone group requiring surgery	30	9	3 in $\leq$ 3 d; 3 in 4–7 d; 3 in $>$ 7 d
Miah et al[39]	16 mg on days 1–4, 8 mg on days 5–7, 4 mg on days 8–10, 2 mg on days 11–13, 1 mg on days 14–16, 0.5 mg on days 17–19, and stopped at day 20, resulting in a total amount of 110.5 mg dexamethasone	19 d	Follow-up CT scan and neurological examination on day 20 after 19 d of dexamethasone therapy or early if dexamethasone was stopped early due to clinical requirement	Architecture (homogenous, laminar, separated, trabecular) and density subtypes of cSDH (hematoma with and without hyperdense components)	85	48	16 d

Abbreviations: cSDH, chronic subdural hematoma; CT, computed tomography.

Table 6 Quality assessment of the included studies according to the Newcastle–Ottawa scale

Sl. no.	Groups	Selection				Comparability	Outcome			Total score
	Study	Representativeness of sample	Selection of the nonexposed cohort	Ascertainment of prognostic variable	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts based on the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts	
1	Sun et al[43]	★		★	★	★	★	★	★	7/9
2	Delgado-López et al[36]	★		★	★	★	★	★	★	7/9
3	Thotakura and Marabathina[44]	★		★	★		★	★	★	6/9
4	Fountas et al[37]	★		★	★	★	★	★	★	7/9
5	Papacocea[41]	★	★	★	★	★	★	★	★	8/9
6	Miah et al[40]	★		★	★		★	★	★	6/9
7	Holl et al[38]	★		★	★	★	★	★	★	7/9
8	Ahmed et al[1]	★		★	★	★	★		★	6/9
9	Miah et al[39]	★	★	★	★	★	★	★	★	8/9

Note: ★ indicates that it meets the criteria in the Newcastle–Ottawa Scale.

found that the neomembrane of the cSDH has plasma cells and macrophages that produce vascular endothelial growth factor (VEGF) and beta fibroblast growth factor (bFGF) that promote angiogenesis, suggesting that cSDH is an angiogenic disease due to a subacute inflammatory response.[48] The potential role of inflammation in the causation of cSDH is the rationale for using steroids to treat cSDH. Glucocorticoids potentially limit the formation of neomembrane by their inhibitory effect on lymphokines and prostaglandins and stimulation of inflammatory inhibitors like lipocortin.[4,49] Glucocorticoids also stimulate plasminogen secretion and inhibit VEGF, interrupting the bleeding–reabsorption–rebleeding cycle in cSDH.[4]

Dexamethasone was used in the current study to assess its efficacy as a stand-alone therapy for the treatment of cSDH and its effect on the requirement for further surgery.[38] In total, 594 individuals who got dexamethasone alone as the primary therapy for cSDH were included in the study's systematic review and meta-analysis of 35 trials.[38] More than one-third of the patients receiving dexamethasone needed further surgery, according to the findings. Larger hematomas and higher MGS ratings showed that these individuals had more severe injuries. Compared to individuals who did not undergo surgery, the OR for needing subsequent surgery was 2.91, indicating a noticeably greater chance.[38] These results imply that a significant fraction of patients still need surgery, even if dexamethasone may help minimize the need for surgery in some people.

A study Qian et al[25] evaluated the risk variables for recurrence of cSDH and discovered that advanced age, midline displacement more significant than 10 mm, and separated hematoma were all related to a higher risk of recurrence. However, they found that postoperative dexamethasone medication lowered the recurrence rate considerably.[25] This shows that dexamethasone may protect against the repetition of cSDH and should be included in the therapeutic strategy.

Numerous traits were also shown in the research[38] associated with a greater likelihood of requiring further surgery. Statin use, a more remarkable midline shift, a larger hematoma thickness, a bilateral hematoma, a separated hematoma, an MGS score of 2, and a bilateral hematoma were among these. Contrarily, the usage of antithrombotic and the existence of trabecular hematoma reduced the likelihood of further surgery.[38] These results provide meaningful data on patient characteristics that could guide treatment decisions and help identify patients who might benefit from early surgical intervention.

Researchers investigated several cSDH treatment approaches in 2005,[43] including dexamethasone alone, surgical drainage with or without dexamethasone, and observation without any kind of therapy. Most patients who were treated with dexamethasone alone had favorable outcomes, with just a tiny minority requiring retreatment. Whether dexamethasone was used during surgery or not, the results were comparable. On the other hand, observation alone had a lower success rate, with only

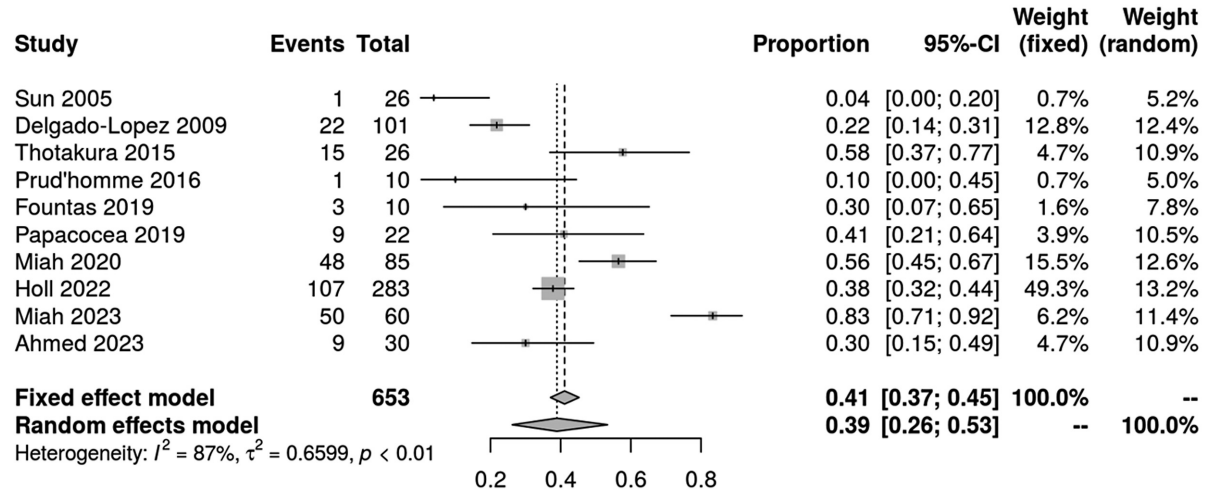

Fig. 2 Forest plot of meta-analysis of proportions for need of surgery in patients with primary dexamethasone therapy. CI, confidence interval.

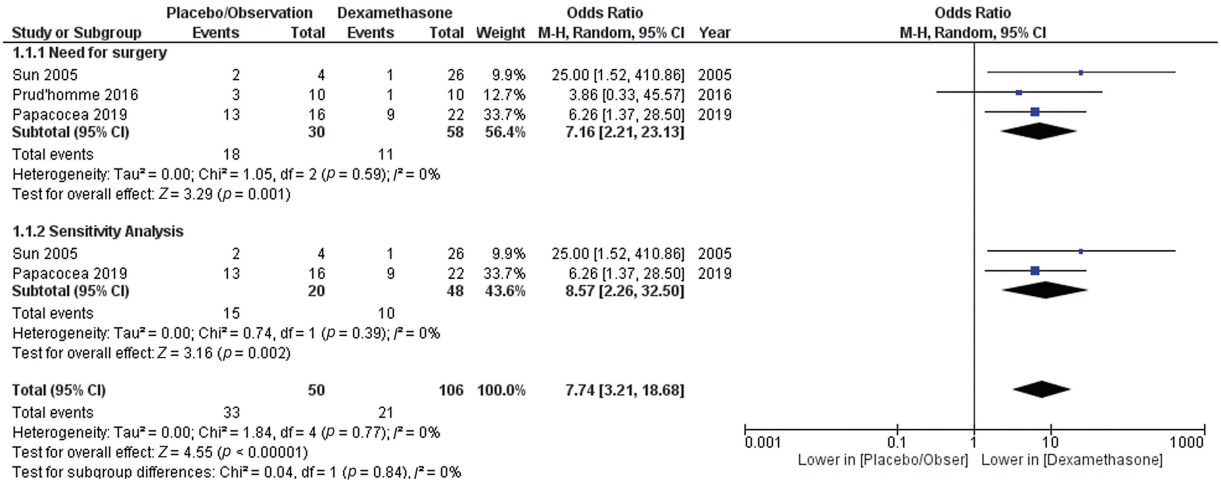

Fig. 3 Forest plot of one-to-one comparison of dexamethasone with placebo/observation. CI, confidence interval.

50% of patients needing surgical drainage.[43] These findings point to dexamethasone's effectiveness as a cSDH treatment option, alone or in combination with surgical drainage.

Delgado-López et al[36] investigated the effectiveness of several treatment modalities in 122 individuals with cSDH. They discovered that dexamethasone alone, subdural drain insertion, and craniotomy all resulted in favorable outcomes in most patients. However, patients with a midline displacement of more than 10 mm and a separated hematoma had a higher risk of recurrence and required reoperation.[36] These findings emphasize the need to consider unique radiological features and patient considerations when determining the best treatment plan for cSDH.

A study by Miah et al[39] looked at dexamethasone as a stand-alone treatment for cSDH in another trial. They included 283 patients, of whom 38% had surgery after receiving one or more rounds of dexamethasone. At 6 months, the research found that 83.9% of patients in the dexamethasone group had a favorable result (mRS score of 0–3) compared to 90.3% in the placebo group, with a statistically significant between-group difference in favor of the placebo group.[39] The findings above underscore the necessity for further investigation and raise skepticism regarding the efficacy of dexamethasone as a sole intervention for cSDH.

Additionally, an RCT was conducted, involving 748 patients, to assess dexamethasone's effectiveness as a treatment for cSDH.[21] The research findings indicated a decreased incidence of positive results (as measured by the mRS score of 0–3) in the cohort receiving dexamethasone in comparison to the cohort receiving placebo after a period of 6 months (83.9 vs. 90.3%). After adjusting for confounders, dexamethasone had an OR of 0.55 for a good result. This shows a considerable placebo advantage.[21] These data suggest that dexamethasone alone may not be as beneficial as thought.

Dexamethasone-treated patients had 84.8% positive outcomes in a prospective cohort trial.[24] Dexamethasone prevented recurrence, whereas placebo caused 20.83%. Period of stay and mRS scores showed no significant differences.[24] These findings indicate dexamethasone's potential efficacy in avoiding recurrence, although its influence on overall clinical results is unknown.

In addition, the effects of various cSDH treatment modalities, such as conservative therapy, burr hole surgery alone, and burr hole surgery in conjunction with dexamethasone, were also studied.[37] The outcome after surgical versus nonsurgical treatment of chronic subdural[37]; group to the other two groups reported that the conservative management group's length of hospital stay was much shorter. However, there were no appreciable variations in the death or recurrence rates across the therapy groups.[37] These findings highlight the necessity of individualized treatment strategies based on the traits and preferences of the patient.

A recent study by Miah et al[40] compared primary surgery without dexamethasone to dexamethasone therapy as an initial treatment for cSDH. According to the researchers, the two therapy groups had no significant difference in functional results or death. Dexamethasone increased cSDH recurrence and reoperation. Dexamethasone patients had comparable hospital stays to open surgery patients.[40] This research found that dexamethasone may improve functional results in the short term but may increase long-term recurrence and surgical intervention.

Papacocea et al[41] compared dexamethasone therapy to observation in cSDH patients. Dexamethasone recipients avoided surgery at 59.1%,compared to 18.7% in the observation group. Dexamethasone field treatment caused hyperglycemia in a small minority of research subjects.[41] However, dexamethasone may reduce surgery. These findings highlight the necessity to monitor and address harmful consequences.

Overall, this study's and other research's findings provide information on the efficacy of dexamethasone as a potential cSDH treatment. Even though dexamethasone may help some patients avoid surgery, a sizable fraction still needs it. Patients who could benefit from early surgical intervention can be identified using traits such as MGS, hematoma features, and comorbidities. However, inconsistent findings from several trials point to the necessity for more investigation to define the function of dexamethasone in individualized treatment plans for cSDH. To enable individualized treatment options for cSDH, future prospective studies should concentrate on identifying individuals who would benefit most from immediate surgery versus those in whom dexamethasone could be an adequate field.[38]

The findings indicate that even while dexamethasone can improve functional outcomes in a sizable fraction of cSDH patients, a significant portion may still need further surgery. There is a greater chance of surgery being necessary if there is an enormous hematoma, a higher midline shift, or statin usage. However, the possibility of subsequent surgery is decreased using antithrombotic and the existence of trabecular hematoma. Remembering that dexamethasone therapy might cause side effects, including hyperglycemia, is crucial. Therefore, based on the patient's clinical features and reaction to the first treatment, treatment recommendations should be tailored to them specifically. Further investigation is necessary to validate these findings and ascertain the optimal treatment approach, specifically by implementing prospective trials involving larger sample sizes. Consequently, treatment recommendations should be customized to suit the patient's clinical characteristics and response to the initial treatment. Further investigation is necessary to corroborate these findings and ascertain the optimal treatment approach for cSDH. This entails conducting prospective studies with larger cohorts.[21,24,25,36–41,43]

Considering the numerous research on the efficacy of dexamethasone for cSDH, while dexamethasone may provide favorable results for a major proportion of patients, a significant number of people still require different surgical surgery. Larger hematoma size, higher midline shift, and statin usage have been linked to an increased risk of surgery. Still, antithrombotic use and the existence of trabecular hematoma have been linked to a decreased likelihood of subsequent surgery.

Given the disparities in the studies' findings, evaluating individual patient features and reactions to the first treatment is critical when deciding the best cSDH method. More research, including larger sample size prospective studies, is required to validate these findings and establish optimal treatment strategies for cSDH.[21,24,37–41] Finally, a personalized therapy strategy that considers patient-specific characteristics will be critical for improving outcomes in cSDH patients.

Limitations and Considerations for Future Research

The inconsistency in the results, as seen from the meta-analysis, is possible because of the differences in the underlying population characteristics, dose, and duration of dexamethasone, for example, in the study by Miah et al.[40] The authors found that the number of patients requiring additional surgery was relatively high (50 of 60). In their research, dexamethasone was given for 12 days. In the study by Holl et al,[38] the number of patients requiring additional surgery was less than that in the survey by Miah et al.[40] In this study, the authors used dexamethasone for a longer duration, a mean of 30 days, and had the protocol of additional dexamethasone in nonresponders.

Holl et al[38] found that patients who had a higher degree of neurological involvement assessed by MGS, bilateral cSDH, larger thickness of the hematoma, use of statins, separated type of cSDH, and more extensive extent of midline shift tend to require additional surgery after therapy with dexamethasone. Minimal knowledge exists on the natural history of cSDH due to the lack of literature. It is understood that cSDH might follow a self-limiting course; however, the pathophysiological process becomes a vicious cycle, demanding some form of mandatory intervention. cSDH, after formation, expands in its thickness and reaches the laminar stage. Following the laminar stage, the neovascular membrane formation accelerated and turned cSDH into a separate pattern and then into the trabecular pattern, after which absorption of cSDH begins. This could explain why more patients with separate cSDH types require surgical intervention.

One crucial issue identified from the present review was that there was no consistency in the dose and duration of dexamethasone therapy. Some studies used a shorter time, smaller quantity, and a single course of dexamethasone. In contrast, others used a more extended period, more significant amount, and multiple methods of dexamethasone therapy. Although most studies reported on the functional outcome, even that differs by the tool used to measure the outcome. Some studies used mRS and MGS at discharge or follow-up, while others used clinical response and the need for additional surgery to measure optimal outcomes. Only a few studies have focused on the radiological development and clinical outcome. The mortality and length of hospital stay were also assessed in these study reports; however, there was heterogeneity in the population. For example, some studies have evaluated the mortality in medical management overall without subdividing the groups into those who did not need surgery after failed medical management. At the same time, some have taken patients with surgery as the primary mode of administration. The recurrence was not uniformly defined in all the studies. Some studies used nonimprovement or worsening radiological profile as recurrence, while some studies defined recurrence as patients who initially improved and then had a recurrence of symptoms. As it is understood that cSDH has heterogeneity in its pathophysiology, considerable heterogeneity has been observed in the studies on managing this enigmatic disease. This restricts achieving evidence of high quality and certainty.

In the study by Papacocea et al,[41] the authors performed a one-to-one comparison of cSDH receiving dexamethasone and not and determining the need for surgery in both the cohorts. The authors found that 40.9% patients who had received dexamethasone needed additional surgery, while 81.3% cSDH patients who did not received dexamethasone required additional surgery. They also found that not only dexamethasone decreased the requirement for surgery in cSDH but it also increased the duration after which surgery was required. Although the findings seem promising and supportive for the use of dexamethasone alternative to surgery, it should be borne in mind that the sample size of the study by Papacocea et al was very small and consisted of only 38 patients. Although the authors ensured that both the groups in their study was homogenous with respect to underlying characteristics and demographics, the decision for surgery could still be biased by the surgeon's decision and other underlying characteristics of cSDH. The low rate of complications and morbidity was attributed by the authors to a lower dose of dexamethasone in their protocol.

Prud'homme et al[42] reported an interesting finding that the hematoma thickness reduced at a faster rate in patients receiving dexamethasone; however, the radiological results at 6 months of follow-up were similar in the dexamethasone group and the placebo group. However, the sample size was very small limiting the generalizability of the results.

Three studies made a one-to-one comparison of the need for surgery between the dexamethasone only group and the placebo or observation group.[41–43] In the study by Sun et al,[43] the sample in the group of observation comprised only four patients. Further there was selection bias in the classification of patients into different groups as the elderly patients with comorbidities were treated with dexamethasone only although the hematoma thickness and cSDH characteristics did not differ significantly among the groups.

In an RCT by Hutchinson et al,[21] the authors found that dexamethasone therapy had worse functional outcome at 6 months than placebo in cSDH. As most patients underwent surgery at the index admission, the trial was not designed to find if dexamethasone therapy could reduce the need for surgery. However, in the trial, there was a group of 38 patients that underwent observation. Of these, 22 received dexamethasone. At 6 months, a favorable outcome was seen in 84% of patients receiving dexamethasone and 100% in patients receiving placebo. This finding and other findings in the literature suggest a possibility that although dexamethasone reduces the need for surgery, it may potentially worsen the long-term functional outcome in cSDH patients. The exact association and underlying mechanisms need larger studies focused on the role of dexamethasone in reducing the need for surgical procedure.

Conclusion

To summarize, the utility of dexamethasone in patients with persistent subdural hematoma is still being determined, and more study is needed. While it may reduce the need for surgery in some cases, many patients still require surgical intervention. The study heterogeneity, small number of RCTs, and absence of standardized methods for dexamethasone administration and dose underline the need for care in interpreting the findings. Future prospective studies with a larger sample size, extended follow-up periods, and standardized treatment regimens are required to improve the discipline. These studies should try to identify the patient subgroups that might benefit the most from various treatment modalities, develop appropriate dose regimes, and assess long-term results. By addressing these research gaps, evidence-based guidelines for clinical practice and improving outcomes in patients with persistent subdural hematoma can be produced.

Funding
None.

Conflict of Interest
None declared.

References

1 Ahmed OEF, Nagaty A, Helmy M, El Molla ST. The use of dexamethasone therapy for conservative management of chronic subdural hematomas: a question about efficacy and safety. Egypt J Neurol Psychiat Neurosurg 2023;59(01):48
2 Kolias AG, Chari A, Santarius T, Hutchinson PJ. Chronic subdural haematoma: modern management and emerging therapies. Nat Rev Neurol 2014;10(10):570–578
3 Kudo H, Kuwamura K, Izawa I, Sawa H, Tamaki N. Chronic subdural hematoma in elderly people: present status on Awaji Island and epidemiological prospect. Neurol Med Chir (Tokyo) 1992;32(04):207–209

4 Santarius T, Hutchinson PJ. Chronic subdural haematoma: time to rationalize treatment? Br J Neurosurg 2004;18(04):328–332
5 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372(71):n71
6 Higgins JP, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, UK:: John Wiley & Sons; 2019
7 Markwalder TM, Steinsiepe KF, Rohner M, Reichenbach W, Markwalder H. The course of chronic subdural hematomas after burr-hole craniostomy and closed-system drainage. J Neurosurg 1981;55(03):390–396
8 Higgins JPT, Altman DG, Gøtzsche PC, et al; Cochrane Bias Methods Group Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928
9 Wells G, Shea B, O'Connell D, et al. Newcastle-Ottawa Quality Assessment Scale Cohort Studies. Ottawa:: University of Ottawa;; 2014
10 AbdelFatah MAR. Medical management of chronic subdural hematoma with low-dose dexamethasone: a case series study. NPG Neurol Psychiatr Geriatr 2023;23(133):29–33
11 Chan DYC, Sun TFD, Poon WS. Steroid for chronic subdural hematoma? A prospective phase IIB pilot randomized controlled trial on the use of dexamethasone with surgical drainage for the reduction of recurrence with reoperation. Chin Neurosurg J 2015;1(01):1–5
12 David RJ, Tan E, Teo MK. Trial of dexamethasone for chronic subdural hematoma. Br J Neurosurg 2023;37(02):241
13 Davis-Wilkie C. A randomised, double blind, placebo-controlled trial of a two-week course of dexamethasone for adult patients with a symptomatic chronic subdural haematoma (Dex-CSDH trial). 2019. Doi: 10.1002/central/CN-01933478
14 Diener HC. Dex-CSDH trial: dexamethasone for chronic subdural hematoma. Arzneimitteltherapie 2021;39(03):84–85
15 Edlmann E, Giorgi-Coll S, Thelin EP, Hutchinson PJ, Carpenter KLH. Dexamethasone reduces vascular endothelial growth factor in comparison to placebo in post-operative chronic subdural hematoma samples: a target for future drug therapy? Front Neurol 2022;13:952308
16 Edlmann E, Thelin EP, Caldwell K, et al; Dex-CSDH trial collaborative and BNTRC collaborative. Dex-CSDH randomised, placebo-controlled trial of dexamethasone for chronic subdural haematoma: report of the internal pilot phase. Sci Rep 2019;9(01):5885
17 Fan Y, Wang D, Rao C, et al. Atorvastatin combined with low-dose dexamethasone treatment protects endothelial function impaired by chronic subdural hematoma via the transcription factor KLF-2. Drug Des Devel Ther 2020;14:3291–3299
18 Fan YS, Wang B, Wang D, et al. Atorvastatin combined with low-dose dexamethasone for vascular endothelial cell dysfunction induced by chronic subdural hematoma. Neural Regen Res 2021; 16(03):523–530
19 Holl D, Miah IP, Blaauw J, et al. Dexamethasone versus burr-hole craniostomy for chronic subdural hematoma; the DECSA trial. Brain Spine 2021;1:100648
20 Huang J, Li L, Zhang J, et al. Treatment of relapsed chronic subdural hematoma in four young children with atorvastatin and low-dose dexamethasone. Pharmacotherapy 2019;39(07):783–789
21 Hutchinson PJ, Edlmann E, Bulters D, et al; British Neurosurgical Trainee Research Collaborative Dex-CSDH Trial Collaborators. Trial of dexamethasone for chronic subdural hematoma. N Engl J Med 2020;383(27):2616–2627
22 Jong JD. Dexamethasone versus burr hole craniostomy for symptomatic chronic subdural hematoma (DECS). 2019. Doi: 10.1002/central/CN-01933494
23 Kolias AG. A randomised, double blind, placebo-controlled trial of a two-week course of dexamethasone for adult patients with a symptomatic chronic subdural haematoma. 2019. Doi: 10.1002/central/CN-01933497
24 Mebberson K, Colditz M, Marshman LAG, Thomas PAW, Mitchell PS, Robertson K. Prospective randomized placebo-controlled double-blind clinical study of adjuvant dexamethasone with surgery for chronic subdural haematoma with post-operative subdural drainage: interim analysis. J Clin Neurosci 2020; 71:153–157
25 Qian Z, Yang D, Sun F, Sun Z. Risk factors for recurrence of chronic subdural hematoma after burr hole surgery: potential protective role of dexamethasone. Br J Neurosurg 2017;31(01):84–88
26 Rudiger A, Ronsdorf A, Merlo A, Zimmerli W. Dexamethasone treatment of a patient with large bilateral chronic subdural haematomata. Swiss Med Wkly 2001;131(25–26):387
27 Saul H, Gursul D, Cassidy S, Hutchinson P, Kolias A. Dexamethasone should not be given to people with a chronic subdural haematoma. BMJ 2022;377:o1302
28 Simon A. Chronic subdural hematoma: is dexamethasone safe and effective? Neurologie Up2date 2021;4(02):111–112
29 Sioutas GS, Mannam SS, Corral Tarbay A, et al. dexamethasone and statins in patients undergoing primary middle meningeal artery embolization for chronic subdural hematoma: a propensity-matched study in the TriNetX research network. World Neurosurg 2023;176:e83–e90
30 Tariq J, Bhatti SN. Adjunctive postoperative course of dexamethasone in chronic subdural hematoma: effect on surgical outcome. Pak J Med Sci 2021;37(07):1877–1882
31 Vetter C. Chronic subdural hematoma: poorer clinical outcome in a therapy with dexamethasone. Dtsch Arztebl Int 2021;118(26): A-1315
32 Wang D, Fan Y, Ma J, et al. Atorvastatin combined with dexamethasone promote hematoma absorption in an optimized rat model of chronic subdural hematoma. Aging (Albany NY) 2021;13(22):24815–24828
33 Wang D, Gao C, Xu X, et al. Treatment of chronic subdural hematoma with atorvastatin combined with low-dose dexamethasone: phase II randomized proof-of-concept clinical trial. J Neurosurg 2020;134(01):235–243
34 Yuan J, Li Y, Liu X, et al. Atorvastatin plus low-dose dexamethasone may be effective for leukemia-related chronic subdural hematoma but not for leukemia encephalopathy: a report of three cases. Front Oncol 2021;11:628927
35 Zhang Y, Chen S, Xiao Y, Tang W. Effects of dexamethasone in the treatment of recurrent chronic subdural hematoma. World Neurosurg 2017;105:115–121
36 Delgado-López PD, Martín-Velasco V, Castilla-Díez JM, Rodríguez-Salazar A, Galacho-Harriero AM, Fernández-Arconada O. Dexamethasone treatment in chronic subdural haematoma. Neurocirugia (Astur) 2009;20(04):346–359
37 Fountas K, Kotlia P, Panagiotopoulos V, Fotakopoulos G. The outcome after surgical vs nonsurgical treatment of chronic subdural hematoma with dexamethasone. Interdiscip Neurosurg 2019;16:70–74
38 Holl DC, Fakhry R, Dirven CMF, et al. Surgery after primary dexamethasone treatment for patients with chronic subdural hematoma: a retrospective study. World Neurosurg 2022;162: e358–e368
39 Miah IP, Blanter A, Tank Y, et al. Change in hematoma size after dexamethasone therapy in chronic subdural hematoma subtypes: a prospective study in symptomatic patients. J Neurotrauma 2023;40 (3–4):228–239
40 Miah IP, Herklots M, Roks G, et al. Dexamethasone therapy in symptomatic chronic subdural hematoma (DECSA-R): a

retrospective evaluation of initial corticosteroid therapy versus primary surgery. J Neurotrauma 2020;37(02):366–372
41 Papacocea T, Popa E, Dana T, Papacocea R. The usefulness of dexamethasone in the treatment of chronic subdural hematomas. Farmacia 2019;67(01):140–145
42 Prud'homme M, Mathieu F, Marcotte N, Cottin S. A pilot placebo controlled randomized trial of dexamethasone for chronic subdural hematoma. Can J Neurol Sci 2016;43(02):284–290
43 Sun TF, Boet R, Poon WS. Non-surgical primary treatment of chronic subdural haematoma: preliminary results of using dexamethasone. Br J Neurosurg 2005;19(04):327–333
44 Thotakura AK, Marabathina NR. Nonsurgical treatment of chronic subdural hematoma with steroids. World Neurosurg 2015;84(06):1968–1972
45 Dran G, Berthier F, Fontaine D, Rasenrarijao D, Paquis P. Effectiveness of adjuvant corticosteroid therapy for chronic subdural hematoma: a retrospective study of 198 cases. Neurochirurgie 2007;53(06):477–482
46 Berghauser Pont LM, Dammers R, Schouten JW, Lingsma HF, Dirven CM. Clinical factors associated with outcome in chronic subdural hematoma: a retrospective cohort study of patients on preoperative corticosteroid therapy. Neurosurgery 2012;70(04):873–880, discussion 880
47 Bender MB, Christoff N. Nonsurgical treatment of subdural hematomas. Arch Neurol 1974;31(02):73–79
48 Vaquero J, Zurita M, Cincu R. Vascular endothelial growth-permeability factor in granulation tissue of chronic subdural haematomas. Acta Neurochir (Wien) 2002;144(04):343–346, discussion 347
49 Glover D, Labadie EL. Physiopathogenesis of subdural hematomas. Part 2: Inhibition of growth of experimental hematomas with dexamethasone. J Neurosurg 1976;45(04):393–397
50 Ito H, Komai T, Yamamoto S. Fibrinolytic enzyme in the lining walls of chronic subdural hematoma. J Neurosurg 1978;48(02):197–200
51 Labadie EL, Glover D. Local alterations of hemostatic-fibrinolytic mechanisms in reforming subdural hematomas. Neurology 1975;25(07):669–675
52 Suzuki J, Takaku A. Nonsurgical treatment of chronic subdural hematoma. J Neurosurg 1970;33(05):548–553

